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كلية الدراسات العليا

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نموذج رقم (١٨)
اقرار والتزام بالمعايير الأخلاقية والأمانة العلمية
وقوانين الجامعة الأردنية وأنظمتها وتعليماتها
لطلبة الماجستير

أنا الطالب: باسل مصطفى سليمان بني هذيل الرقم الجامعي: (٨٠٦٠٣٨٠)

تخصص: الكيمياء العضويه الكليـــــــة:العلوم

عنوان الرسالة:

MICROWAVE ASSISTED SYNTHESIS OF SOME NEW IMIDAZOLYL QUINOLINE COMPOUNDS

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التوقيع.......التاريخ.......

MICROWAVE ASSISTED SYNTHESIS OF SOME NEW IMIDAZOLYL QUINOLINE COMPOUNDS

By
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This Thesis was submitted in Partial Fulfillment of the Requirements

For the Master`s Degree of Science in Chemistry

Faculty of Graduate Studies

The University of Jordan

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Committee Decision

This Thesis (Microwave assisted synthesis of some new imidazolyl quinoline compounds) was successfully defended and approved on Thursday 04 – August - 2011

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Dedication

To my family

Father, Mother,

Brothers, Sisters,

And

To my beloved wife Shereen

Acknowledgements

Words cannot express how grateful I am towards our Almighty Allah whom without had I not reached to the success I shall cherish forever.

I want to express my deepest gratitude and sincere appreciation to Dr. Raed A. Al-Qawasmeh and Prof. Dr. Musa H. Abu Zarga for their direct supervision, guidance and encouragement during the course of this work.

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All my thanks and love to my father, mother, brothers and sisters who have given me light of hope to accomplish my goal by their encouragement and support.

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2D : Two Dimensional.

COSY : Correlated Spectroscopy.

DEPT : Distortionless Enhancement by Polarization Transfer.

HIV : Human Immunodeficiency Virus.

HMBC : Heteronuclear Multiple Bond Connectivity.

HMQC : Heteronuclear Multiple Quantum Coherence.

HRMS : High Resolution Mass Spectrometry.

MAOS : Microwave assisted organic synthesis.

MS : Mass Spectrometry.

MW : Microwave.

NMR : Nuclear Magnetic Resonance spectrometry.

TLC : Thin Layer Chromatography.

DMSO : Dimethylsulfoxide.

DCM : Dichloromethane.

PQ : Pyrazoloquinoline.

ESI : Electrospray Ionization.

RNA : Ribonucleic Acid.

DNA : Deoxyribo Nucleic Acid.

PCC : Pyridinium chlorochromate.

TMS : Tetramethylsilane.

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Abstract

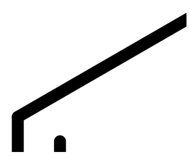
Microwave assisted organic synthesis (MAOS) has emerged as an efficient and simple technique for enhancing the yield and reducing the time for chemical reactions. In this study, a new library of compounds was designed based on bioactive chromophors, the newly synthesized imidazolylquinoline library was carried out using the microwave reactor, compounds were characterized using various spectroscopic techniques such as ^{1}H-NMR, ^{13}C-NMR, 2D -NMR (HMQC and HMBC) and mass spectrometry.

1. Introduction

1.1. Quinoline

1.1.1. Importance and applications of quinolines.

Quinoline **(1)** is a heterocyclic aromatic organic compound scaffold of paramount importance to human race. It has the formula C_9H_7N and is a colourless hygroscopic liquid with a strong odour. The utility of quinoline derivatives in the areas of medicine, food, catalysis, dye materials, refineries and electronics is well established. As a result, the synthesis of quinoline core and its derivatives have been an attractive goal for the synthetic organic chemist.

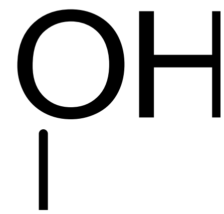


In pursuit to develop easy and practical approaches to a variety of quinoline derivatives decorated with useful pharmacophores, different research groups developed a well established synthetic methodologies toward the synthesis.

Compounds containing quinoline motif are most widely used as:

1- Antimalarials.

Many quinoline derivatives proved to have antimalarial activity e.g. compounds **2, 3** and **4** **(** Billker *et al*., 1998).



2- Antibacterials.

Many quinoline containing compounds showed antibacterial activities. For example quinoline-4-carboxylic acid like 2-(1-chloro-2-fluoroethylthio)-6,7-difluoro-4-((R)-2-phenylpropanoyloxy)-quinoline-3 carboxylic acid **(5)** showed excellent *in vitro* and *in vivo* antibacterial activity (Matsuoka *et al*., 1999).

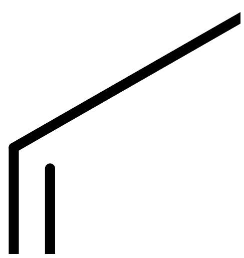
3- Antifungals

The compounds bearing a quinoline moiety such as 8-hydroxyquinoline **(6)** and its derivatives e.g. **(7)** were introduced into antifungal clinical use (Musiol *et al.,* 2006) (Gershon *et al*., 2004), (Dardari *et al*., 2004), (Jampilek *et al*., 2005). A series of compounds derived from 8-hydroxyquinoline as potential HIV-1 integrase inhibitors were synthesized recently e.g. compound **8** (Majerz-Maniecka *et al.,* 2005) (Majerz-Maniecka *et*

al., 2011). These compounds show a significant similarity to the novel antifungal agents, homoallylamines, which possess potent antifungal activity (Vargas *et al.*, 2003).

4- Anticancer agents

Some of the quinoline derivatives showed appreciable anti-cancer activities, such as **9** (Singh *et al*., 2007).



5- Other uses

Quinoline derivatives find use in the synthesis of fungicides, virucides, biocides, rubber chemicals and flavoring agents. For example 4-amino- 1-[8-(trifluoromethyl)quinolin-4-yl]-1*H*-pyrazolo[3,4- d]pyrimidine **(10)** exhibited very good activity against *A. flavus*, *A. fumigatus*, and *T. mentagrophytes* (Holla *et al*., 2006).

Also, some quinolines are used as polymers, catalysts, corrosion inhibitors and preservatives. Furthermore, these compounds find applications in chemistry of transition-metal catalysts for uniform polymerization and luminescence chemistry. Among the organic materials, considerable interest has been given to pyrazoloquinoline (PQ) [1H-pyrazolo[3,4-b]quinoline] **(11)** which recently has been found as a highly efficient fluorescent dopant for polymer matrixes used in electroluminescent applications (Calus *et al*., 2006).

1.1.2. Syntheses of quinoline

The quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmacological properties. Many reviews were published describing quinoline syntheses (Kouznetsov *et al*., 2005) (Yamashkin *et al*., 1992) (Michael, 2004).

The most important methods from quinoline moieties synthesis are:

1.1.2.1. Skraup reaction

Scheme 1 shows the skraup reaction, in which aniline **(12)** and glycerol **(13)** are heated in the presence of sulfuric acid and an oxidizing agent, like nitrobenzene to form unsubstituted quinolines.



Scheme 1. Synthesis of quinoline *via* Skraup reaction.

1.1.2.2. Combes Synthesis

In Combes quinoline synthesis the condensation of unsubstituted aniline **(12)** with β-diketone **(14)** form substituted quinoline **(16)** after an acid-catalyzed ring closure of an intermediate Schiff base **(15)** as shown in scheme 2.

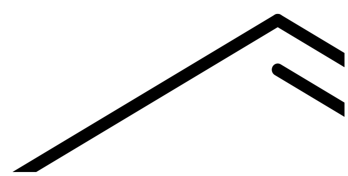
Scheme 2. Synthesis of quinoline *via* combes.

Recently, due to the great biological importance of substituted quinolines, interesting works on this method have extended the scope of this reaction. Microwave-assisted reactions between anilines and alkyl vinyl ketones or 1,3-diketones on the surface of diverse absorbents proceeded smoothly to give new substituted quinolines. A simple and efficient procedure, described by Ranu and co-workers, consists of a one-pot reaction of anilines **(12)** with methyl vinyl ketone or its analogs, for example (*E*)-3-methyl-4-phenylbut-3-en-one **(17)** on the surface of silica gel impregnated with indium(III) chloride under microwave irradiation without any solvent produced 3,4-dimethyl-2-Phenylquinoline **(18)** as shown in scheme 3 (Ranu *et al.,* 2000), (Jiranusornkul *et al*., 2002), (Kidwai *et al.*, 2000).

Scheme 3. Microwave Synthesis of quinoline *via* combes method

1.1.2.3. Friedländer synthesis

Friedländer prepared quinoline in 1882 (Wu *et al*., 2006) by the condensation of *o*-aminobenzaldehyde **(19)** with acetaldehyde **(20)** in the presence of sodium hydroxide as shown in scheme 4 . This type of reaction has since been extensively explored and, in its most general form, can be defined as an acid- or base-catalyzed condensation followed by a cyclodehydration between an o-amino-substituted aromatic aldehyde, ketone, or derivative thereof with an appropriately substituted aldehyde, ketone, or other carbonyl compound containing a reactive α-methylene group. Some quinolines can also be prepared simply by heating a mixture of the reactants with or without a solvent.



Scheme 4. Preparation of quinoline *via* Friedländer synthesis.

Because both reactants contain a carbonyl group, certain quinolines can be prepared from a single starting compound. Of historic interest is the formation of the dye flavaniline **(24)** from acetanilide **(21).** When acetanilide is heated with zinc chloride, the acetyl group of some molecules migrates to the *ortho* position **(22),** and that of others migrates to the *para* position **(23).** The resulting mixture of **(22)** and **(23)** then undergoes Friedländer condensation to form **(24)** as shown in scheme 5.

Scheme 5. Preparation of flavaniline (**24**) *via* Friedländer synthesis from a single starting compound.

1.1.2.4. Doebner-Miller reaction

The Doebner-Miller reaction is the reaction of an aniline with α,β-unsaturated carbonyl compounds to form quinolines. This reaction is also known as the Skraup-Doebner-Von Miller quinoline synthesis. Skraup described heating a mixture of nitroethane, aniline, and glycerol with concentrated sulfuric acid to form quinoline in a very low yield (Jones, 1977), (Manske and Kulka., 1953), (Skraup, 1881. a & b). Subsequently, Doebner and Von Miller replaced the glycerol with an α,β-unsaturated ketone **(27)** and acetone **(26)** and conducted the reaction by heating with an aromatic amine in the presence of an acid catalyst or iodine (Scheme 6) (Doebner and Miller., 1881). The Skraup-Doebner-Von Miller synthesis of quinolines can be catalyzed by Lewis acids such as $SnCl_4$, $Yb(OTf)_3$, $Sc(OTf)_3$, $ZnCl_2$, $InCl_3$, TsOH, $HClO_4$, Amberlite and iodine (Arduini *et al*., 1981),(Glinka., 1965),(Badger, 1963).



Scheme 6. Preparation of quinoline *via* Doebner-Miller reaction.

1.1.2.5. Pfitzinger reaction.

The formation of derivatives of 4-quinolinecarboxylic (cinchoninic acid) as a result of the reaction of isatin or its derivatives with ketones containing the –CH_2CO– group in the presence of sodium hydroxide or potassium hydroxide was first discovered at the end of the nineteenth century by Pfitzinger (Pfitzinger, 1886) (Shvekhgeimer, 2004) and is known in organic chemistry as the Pfitzinger reaction. Pfitzinger first reported the synthesis of 2-methyl-4 quinolinecarboxylic acid **(30)** as a result of the reaction of isatin **(29)** with acetone in the presence of an aqueous solution of alkali as shown in scheme 7.

Scheme 7. Preparation of quinoline *via* Pfitzinger reaction.

1.1.2.6. Conrad-Limpach reaction

The synthesis of 4-quinolones, which often isomerize (or aromatize) to 4-hydroxyquinolines through the thermal condensation of primary aromatic amines with the carbonyl group of β-ketoesters followed by the cyclization of Schiff base intermediates (alkyl β-arylaminocrotonates), is generally known as Conrad–Limpach quinoline synthesis (Reitsema., 1948) . As an example, aniline reacts with ethyl-2-methyl-3-oxobutanoate **(31)** to give 2,3-dimethyl-4-hydroxyquinoline **(33**) *via* the intermediate (Z)-ethyl-2-metyl-3-(phenylimino)butanoate **(32)** as shown in scheme 8.

Scheme 8. Preparation of quinoline *via* Conrad-Limpach reaction.

1.2. Imidazole

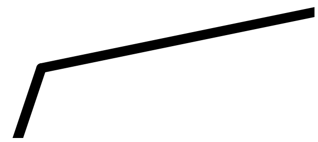
1.2.1. Importance and applications of imidazole

Imidazole **(34)** is an organic compound with the formula $C_3H_4N_2$. Imidazoles are a class of heterocycles with similar ring structure, but varying substituents. This ring system is present in important biological building blocks, such as histidine, and the related hormone histamine. Imidazole can serve as a base and as a weak acid, and it can exists in two equivalent tautomeric forms, 1*H*-imidazole and 3*H*-imidazole, because the hydrogen atom can be located on either of the two nitrogen atoms. The compound is classified as aromatic due to the presence of a sextet of π-electrons, consisting of a pair of electrons from the protonated nitrogen atom and one from each of the remaining four atoms of the ring. Figure **1**, shows some resonance structures of imidazole.



Figure 1. Resonance structures of imidazole.

The presence of imidazole moiety in the amino acid Histamine **(35)** and in part in nucleic acid bases adenine **(36)** and guanine **(37)** makes it a very important moiety.

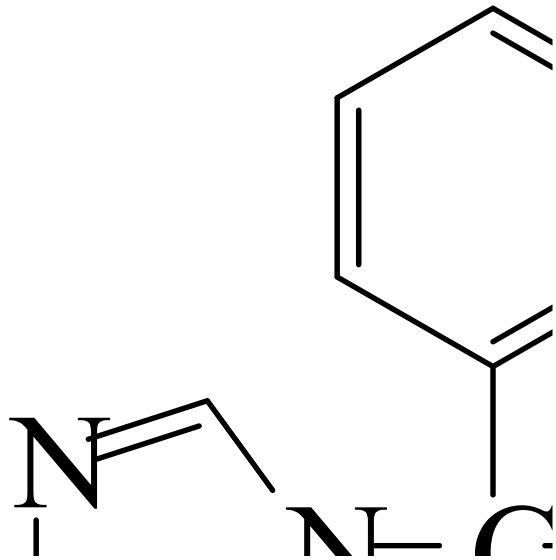


Biologically, compounds containing imidazoles exhibits very good and diverse activities such as.

1. Antifungal and anti bacterial activity

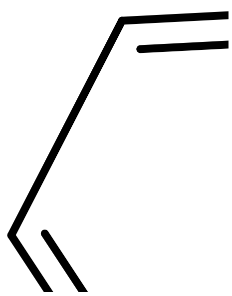
Many compounds containing the imidazole moiety such as clotrimazole **(38),** econazole **(39)** and miconazole **(40)** exhibit excellent antifungal activities (Bhatnagar *et al.*, 2011).

These compounds own their activities to the imidazole moiety, removal of this moiety will demolish the activity. Many other imidazole containing compounds proved to be very potent antibacterial agents, **(41)** for example has a very good activity against multidrug resistance bacterial strains (Al-Qawasmeh *et al*., 2010).



2. Anti -inflammatory and analgesic activity.

2-Substituted-4, 5-diphenyl-1*H*-imidazoles such as **42** show an excellent anti-inflammatory activity (Puratchikodya and Doble., 2007) .

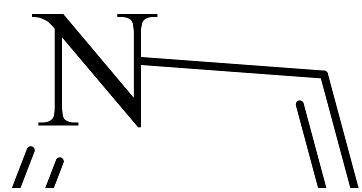


3. Anti-tubercular activity.

A series of compounds derived from benzimidazoles were synthesized recently e.g. **43**. These compounds show an excellent anti-tubercular activity (Shingalapur *et al*., 2009). The compounds bearing imidazole moiety and its derivatives were introduced into anti-tubercular clinical use.

4. Antidepressant activity.

Many imidazole containing compounds showed antidepressant activity. Some of them were synthesized as moclobemide analogues **45** by replacing moclobemide phenyl ring with substituted imidazole to produce a more potent compound such as **44** (Hadizadeh *et al.*, 2008).



5. Anticancer activity.

Many novel compounds containing imidazole moiety e.g. **46** were synthesized in order to investigate thier anticancer activity. Anticancer activity screening results revealed that these compounds were very active (Oezkay *et al.*, 2010). Many other triarylsubstituted imidazoles, showed excellent anticancer activities such as **47** (huesca *et al.*, 2005)

6. Antiviral activity.

Many of 2-phenylbenzimidazole derivatives such as **48** were synthesized and evaluated as antiviral agents. These derivatives proved to be more active than the antiviral drugs smycophenolic acid **49** and 6-azauridine **50.** (Tonelli *et al*., 2010).

7. Antilishmanial activity

A series of substituted aryloxy alkyl and aryloxy aryl alkyl imidazole e.g. **51** were synthesized and evaluated as antileishmanial agents against *Leshmania donovani*. All compounds exhibited 94–100% inhibition (Bhandari *et al*., 2010).

1.2.2. Syntheses of Imidazoles

Imidazoles were prepared in 1858 from glyoxal and ammonia (Siddiqui *et al.*, 2005). Several approaches are available for synthesis of imidazoles such as, Radiszewski synthesis, dehydrogenation of imidazolines, from alpha halo ketones, Wallach synthesis,

from aminonitrile and aldehyde and Marckwald synthesis. Details of the synthetic procedures are given below:

1.2.2.1. Radiszewski synthesis

This method stands on condensing a dicarbonyl compound such as glyoxal, α-keto aldehyde or a- diketones with an aldehyde in the presence of ammonia. Benzil **52**, for instance, reacts with benzaldehyde **53** and two molecule of ammonia to yield 2,4,5-triphenylimidazole **54** as in scheme 9 **(**Lunt *et al.*, 1987) (Hoffman.., 1953) (Bredereck *et al*., 1959)**.**



Scheme 9: Preparation of the imidazoles *via* Radiszewski synthesis.

1.2.2.2. Dehydrogenation of imidazolines.

The imidazole moiety can be prepared from imidazolines *via* dehydrogenation. For example imidazoline obtained from alkyl nitriles **56** and 1, 2 ethanediamine **55** can be reacted with $BaMnO_4$ to yield 2-substituted imidazoles as in scheme 10 (Elderfield., 1957).



Scheme 10. Preparation of imidazoles *via* dehydrogenation of imidazolines.

1.2.2.3. From α-haloketones

This reaction involves an interaction between an imidine and alpha halo ketones. This method has been applied successfully for the synthesis of 2, 4- or 2, 5-biphenyl imidazoles phenacyl bromide and benzimidine according to this method afford 2,4-diphenyl imidazole **(57).** Similarly, amidine reacts with acyloin or alpha halo ketones to yield imidazoles as in scheme 11. (Elderfield**,** 1957).

Scheme 11. Preparation of imidazoles from α-haloketone.

1.2.2.4. Wallach synthesis

When N,N`-dimethyloxamide **(55)** is treated with phosphorus pentachloride, a chlorine containing compound is obtained, which on reduction with hydroiodic acid gives N-methyl imidazole (**56**) as in scheme 12 (Elderfield, 1957) (Wallach and Schuelze., 1881) **(**Wallach and Schuelze., 1880) (Sarasin and Weymann., 1924).



Scheme 12. Preparation of imidazoles *via* Wallach synthesis

1.2.2.5. From aminonitrile and aldehyde

Reaction of aldehyde with aminonitrile produces 2,4-di-substituted imidazoles as in scheme 13

Scheme 13. Production of substituted imidazoles from aminonitrile and aldehyde.

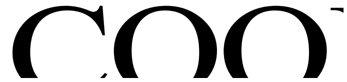
1.3. Microwave in organic synthesis

Microwaves are electromagnetic radiation in the frequency range 0.3–300 GHz (wavelengths of 1 mm to 1 m), between infrared radiation and radio frequencies. In the recent years microwave assisted organic synthesis (**MAOS**) has emerged as a new "lead" in organic synthesis and widely used as a source of heating. Figure (2) shows one of many microwaves used in organic synthesis named Biotage initiator, which was used in the course of this study. Since the first published reports on the use of microwave irradiation to carry out organic chemical transformations by the group of Gedye (Gedye *et al.,* 1986), in the 1990s several groups started to experiment with solvent-free microwave chemistry (so-called dry-media reactions), which eliminated the danger of explosions (Varma, 2002).

Enormous publications reported the use of this technique in all fields of chemistry. The basic mechanisms observed in microwave assisted synthesis are dipolar polarization and conduction. The technique has provided the momentum for many chemists to switch from traditional heating methods to microwave assisted chemistry (**MAOS**). As a result, MW technique has rapidly gained acceptance as a valuable tool for accelerating drug discovery and development processes. (Anastas and Warner, 1998) (Lancaster, 2002) (Nagariya *et al.*, 2010).

Advantages and disadvantages

Time and yield are the main important factors for any chemical reaction. The reduction of time and the enhancements of the yield for the reaction performed with the microwave technology gaves this technology more advantages over the traditional methods. For example esterification of 2-phenylquinoline-4-carboxylic acid **60** with ethanol in the presence of a catalytic amount of concentrated sulphuric acid under MW in a closed Teflon vessel required 10 min to afford ethyl 2-phenylcinchoninate **61** in 94 % yield; under the conventional conditions the reaction required heating under reflux for 22 h to give a comparable yield (Gansser and Rumpf, 1953). Under MW activation, the ester **61** was transformed into the corresponding acid hydrazide **62** in a much shorter time (6 min) compared to conventional heating (15.5 h). Furthermore, the yield of **62** (scheme 14) was improved to 80 % compared with 61 % (Gansser and Rumpf, 1953). MW was used in reaction of isatin with cyclohexanone to produce 1,2,3,4-tetrahydroacridine-9-carboxylic acid **63** in 95 % yield within 12.5 min, but under conventional heating, the reaction required 72 h and gave only a 55 % yield (Al-Tai and Sarkis., 1963) as in scheme 15 .



Scheme 14. Preparation of acid hydrazide (**62**) under microwave irradiation.

Scheme 15. Preparation of 1,2,3,4-tetrahydroacridine-9-carboxylic acid (**63**) under microwave irradiation.

Small amount of reactant for the reactions using the microwave technology can be considered as the only disadvantage of this technology, yet this can be eliminated with further development of this technology.

The advantages of microwave over the conventional heating can be summarized as follows:

· Uniform heating occurs throughout the material

· High efficiency of heating

· Reduction of unwanted side reactions

· Purity of final product

· Improve reproducibility

· Environmental heat loss can be avoided

· Reduce wastage of heating reaction vessel

· Low operating cost



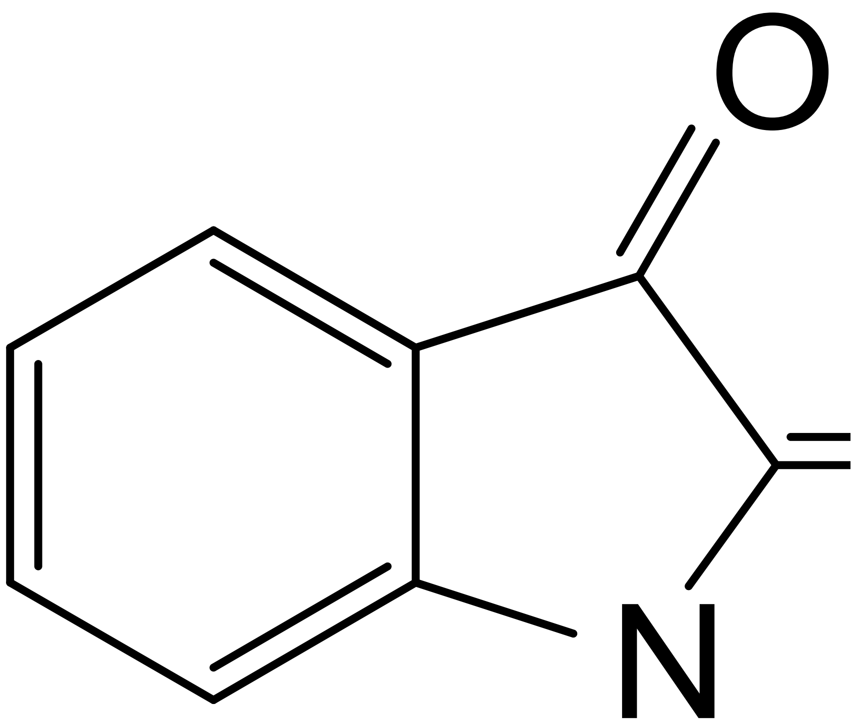
Figure 2. Biotage initiator used in MAOS

2. Purpose the present work

Trisubstituted imidazole compounds with the indole moiety at position 2 of the imidazole ring were shown to possess a potent activity against multidrug resistance bacteria. (Al-Qawasmeh, *et. al*., 2010). In this regard we believe that using the quinoline chromophore as a replacement of indole moiety might produce compounds with better pharmacological properties (Scheme 1).

Scheme 16. The strategy of the research project: replacement of the indole moiety with the quinoline moiety keeping the imidazole with the substituents on positions 4 and 5.

This work is designed to build a new library of compounds which contains the imidazole and the quinoline moieties. A library of forty compounds is designed and execute with the help of microwave technology of synthesis. The synthesis of this library takes the advantages of easy method and available chemicals. The following Scheme shows the general synthetic plan used to produce the new library.


O
N

3. Experimental

3.1. Materials and equipment

Isatin, SeO_2, acetophenone, *p*-methylacetophenone, *p*-fluoroacetophenone, *p*-chloroacetophenone, 1,2-diketones were purchased from Acros, chemicals. Thick layer chromatographic plates (TLC) were made using silica gel (Macherey-nagel GmbH and Co.KG). Melting points were measured by Fischer-Johns Melting Point Apparatus and were uncorrected. ^{1}H- and ^{13}C- NMR spectra were measured on a Bruker DPX-300 instrument. Chemical shifts (δ) are expressed in ppm with reference to *TMS* as internal standard. High resolution mass spectra (HRMS) were measured in positive ion mode by Electrospray Ionization (ESI) on a Bruker instrument. The samples were dissolved in acetonitrile, diluted in spray solution (methanol/water 1:1 v/v + 0.1% formic acid) and infused using a syringe pump with a flow rate of 2 μL/min. External calibration was conducted using Arginine cluster in a mass range *m/z* 175-871. For all HRMS data, mass error: 0.00-0.50 ppm.

3.2. Synthesis

3.2.1. General procedure for preparation of 2-aryl- quinoline -4-carboxylic acids (64a-d)

These acids were synthesized according to the published method (El Ashry *et al.*, 2005). Scheme 14 shows this synthesis in which the conventional and microwave methods were used

a- Conventional method

Isatin **(29)** (1 mmol), acetophenone derivative (1.1 eq.), and 85% KOH (102 mmol) were dissolved in EtOH (40 mL), and the reaction mixture was stirred at 80 °C for 24 h. The mixture was concentrated using rotary evaporator, diluted with ice water, and acidified with concentrated HCl. The resulting precipitate was collected, washed with water, air dried and then recrystallized from ethanol. Generally, yield was between 80-85%.

b- Microwave method

A mixture of isatin (3.4 mmol), acetophenone derivative (1.05 eq), and potassium hydroxide (0.63 g, 11 mmol) in 20% aqueous ethanol (2 ml) was placed in a closed Teflon vessel and irradiated by MW with variable power to keep a constant temperature at 130 ºC for 12 min. The reaction mixture was acidified with acetic acid and the product was recrystallized from EtOH.

Using this general procedure (procedure b), the following compounds were prepared:

2-Phenylquinoline-4-carboxylic acid (64a)

Yield; 96%, white solid, m.p = 214-215 ºC (lit. m.p 212– 214 ºC) (DuPuis and Lindwall, 1934).

HRMS (ESI): calcd. for $C_{16}H_{10}NO_2$ $[M-H]^-$: 248.07115, found: 248.07170.

^{1}H NMR (DMSO-d$_6$): δ 13.95 (bs, 1H ,COO*H*), 8.63 (dd, *J* = 8.5 Hz, *J* = 0.8 Hz, 1H, H-5), 8.43 (s,1H, H-3), 8.27 (dd, *J* = 8.3 Hz, *J* = 1.8 Hz, 2H, H-2`/H6`), 8.14 (dd, *J* = 7.8 Hz, *J* = 0.6 Hz, 1H, H-8), 7.80-7.85 (m, 1H, H-7), 7.65-7.70 (m, 1H, H-6), 7.58 -7.78 (m, H-3`/H-4`/H-5`).

^{13}C NMR (DMSO-d$_6$): δ 168.1 (*C*OOH), 156.3 (C-2), 148.9 (C-8a), 138.4 (C-1`), 138.1 (C-4), 130.7 (C-7), 130.5 (C-4`), 130.3 (C-8), 129.5 (C-2`/C-6`), 128.3 (C-6), 127.7(C-3`/C-5`), 125.9 (C-5), 123.9 (C-4a), 119.6 (C-3).

2-(4-Chlorophenyl)quinoline-4-carboxylic acid (64b).

Yield; 97%, brown solid, m.p = 258-260 ºC (lit. m.p 230-232 ºC) (Wang *et al*., 2009) .

HRMS (ESI): calcd. for $C_{16}H_9ClNO_2$ [M-H]$^-$: 282.03218, found: 282.03273 .

^{1}H NMR (DMSO-d$_6$): δ 8.61 (d, *J* = 7.9 Hz, 1H, H-5), 8.39 (s,1H, H-3), 8.22 (d, *J* = 8.6 Hz, 2H, H-2`/H-6`), 8.07 (d, *J* = 8.1 Hz, 1H, H-8), 7.78 (m, 1H, H-7), 7.63 (m, 1H, H-6), 7.52 (d, *J* = 8.6 Hz, 2H , H-3`/H-5`).

^{13}C NMR (DMSO-d$_6$): δ 168.0 (*C*OOH), 155.0 (C-2), 148.8 (C-8a), 138.1 (C-1`), 137.1 (C-4), 135.4 (C-4`), 130.7 (C-7), 130.3 (C-8), 129.4 (C-2`/C-6`), 128.4(C-3`/C-5`), 128.4 (C-6), 125.9 (C-5), 124.0 (C-4a), 119.5 (C-3).

2-*p*-Tolylquinoline-4-carboxylic acid (64c)

Yield; 99 %, white solid, m.p 225-227 ºC (lit. m.p 242 ºC) (Obushak *et a*l., 2006) .

HRMS (ESI): calcd. for $C_{17}H_{14}NO_2$ $[M+H]^+$: 264.10245, found: 264.10191 .

^{1}H NMR (DMSO-d$_6$): δ 8.61 (d, *J* = 7.8 Hz, 1H, H-5), 8.40 (s,1H, H-3), 8.16 (d, *J* = 8.2 Hz, 2H, H-2\`/H-6\`), 8.11 (d, *J* = 8.0 Hz, 1H, H-8), 7.77-7.83 (m, 1H, H-7), 7.62-7.67(m, 1H, H-6), 7.34 (d, *J* = 8.0 Hz, 2H, H-3\`/H-5\`), 2.35 (s, 3H, CH_3).

^{13}C NMR (DMSO-d$_6$): δ 168.2 (*C*OOH), 156.2 (C-2), 148.9 (C-8a), 140.3 (C-1\`), 138.2 (C-4), 135.6 (C-4\`), 130.7 (C-7), 130.1 (C-8), 130.2(C-2\`/C-6\`), 128.1 (C-6), 127.6 (C-3\`/C-5\`), 125.9 (C-5) , 123.9 (C-4a), 119.4 (C-3), 21.4 (*C*H3).

2-(4-Fluorophenyl)quinoline-4-carboxylic acid (64d)

Yield; 82 %, yellowish solid, m.p = 198 - 199 ºC (lit. m.p 197 ºC) (Buu *et al*., 1949).

HRMS (ESI): calcd. for $C_{16}H_9FNO_2$ $[M-H]^-$: 266.06173, found: 266.06228 .

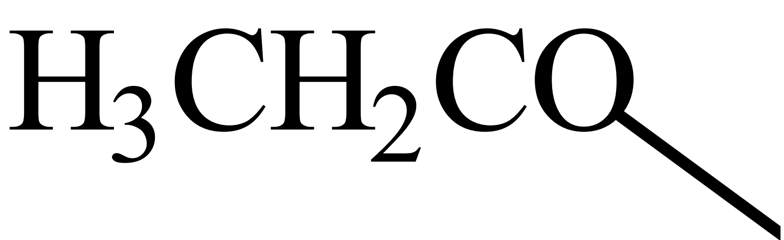
^{1}H NMR (DMSO-d$_6$): δ 8.62 (d, *J* = 7.8 Hz, 1H, H-5), 8.40 (s, 1H, H-3), 8.22 (dd, *J* = 8.9 Hz, *J* = 5.5 Hz , 2H, H-2`/H-6`), 8.09 (d, *J* = 8.4 Hz, 1H, H-8), 7.76-7.81 (m, 1H, H-7), 7.61-7.67 (m, 1H, H-6), 7.32 (t, *J* = 8.9 Hz, 2H , H-3`/H-5`).

^{13}C NMR (DMSO-d$_6$): δ 168.1(*C*OOH), 163.9 (d, $^{1}J_{C\text{-}F}$ = 245 Hz, C-4`), 155.2 (C-2), 148.7 (C-8a), 138.1(C-4), 134.8 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz, C-1`), 130.7 (C-7), 130.1 (C-8), 130.0 (d, $^{3}J_{C\text{-}F}$ = 8.6 Hz, C-2`/C-6`), 128.2 (C-6), 125.9 (C-5), 123.9 (C-4a), 119.5 (C-3), 116.3 (d, $^{2}J_{C\text{-}F}$ = 21.5 Hz, C-3`/C-5`).

3.2.2. General procedure for preparation of ethyl 2-arylquinoline -4-carboxylates (65a-d)

A mixture of compound (**64a-d**) (2.02 mmol), ethyl alcohol (3 ml), and concentrated sulfuric acid (0.5 ml) was placed in a closed Teflon vessel and irradiated by MW with variable power to keep a constant temperature at 80 ºC for 10 min (scheme15). The mixture was neutralized with sodium bicarbonate solution and the product was extracted using EtOAc (2×10 ml). The organic layer was dried over anhydrous Na_2SO_4, filtered, and the solvent evaporated. Using the same general procedure, the following compounds were prepared:

Ethyl 2-phenylquinoline-4-carboxylate (65a)



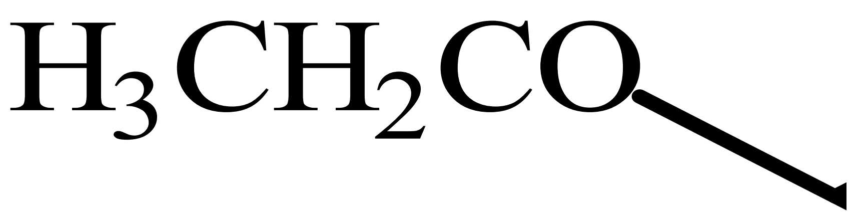
Yield; 60% , yellowish oil, (lit. mp 56–58 ºC) (El Ashry *et al.*, 2005).

HRMS (ESI): calcd. for $C_{18}H_{16}NO_2$ $[M+H]^+$: 278.11810, found: 278.11756.

^{1}H NMR (DMSO-d$_6$): δ 8.73 (d, *J* = 8.5 Hz, 1H, H-5), 8.36 (s, 1H, H-3), 8.21(d, *J* = 8.5 Hz, 2H, H-2`/H-6`), 8.11 (d, *J* = 8.1 Hz, 1H, H-8), 7.80-7.85 (m, 1H, H-7), 7.68 (dt, *J* = 8.3 Hz, *J* = 1.3 Hz, 1H, H-6), 7.50-7.58 (m, H-3`/H-4`/H-5`), 4.48 (q, *J* = 7.1 Hz, 2H, CH_2), 1.39 (t, *J* = 7.1 Hz, 3H, CH_3).

^{13}C NMR (DMSO-d$_6$): δ 166.4 (*C*OOEt), 156.3 (C-2), 148.8 (C-8a), 138.3 (C-1`), 137.2 (C-4), 130.9 (C-7), 130.6 (C-4`), 130.4 (C-8), 129.5 (C-2`/C-6`), 128.5 (C-6), 127.7 (C-3`/C-5`), 125.6 (C-5), 123.6 (C-4a), 119.7 (C-3), 62.4 (CH_2), 14.6 (CH_3).

Ethyl 2(4-chlorophenyl)quinoline-4-carboxylate (65b)



Yield; 74.3%, brownish solid, m.p = 77-80 ºC (lit. mp 72–73 ºC) (Leardin *et al*., 1984).

HRMS (ESI): calcd. for $C_{18}H_{15}ClNO_2$ $[M+H]^+$: 312.07913, found: 312.07858 .

^{1}H NMR (DMSO-d$_6$): δ 8.48 (d , *J* = 8.0 Hz ,1H, H-5), 8.37 (s,1H ,H-3), 8.25 (d, *J* = 8.6 Hz, 2H, H-2`/ H-5`), 8.09 (d, *J* = 8.0 Hz, 1H, H-8), 7.80 (d, *J* = 6.3 Hz, 1H, H-7), 7.67 (d, *J* = 7.6 Hz, 1H, H-6), 7.55 (d, *J* = 7.2 Hz, 1H, H-3`/ H-5`), 4.45 (q, *J* = 6.7 Hz , 2H, OCH_2CH_3), 1.39 (t, *J* = 6.7 Hz, 3H, OCH_2CH_3).

^{13}C NMR (DMSO-d$_6$): δ 166.2 (*C*OOEt), 154.9 (C-2), 148.7 (C-8a), 137.2 (C-1\`), 136.9 (C-4), 135.5 (C-4\`), 130.9 (C-7), 130.3 (C-8), 129.4 (C-2\`/C-6\`/C-6), 128.6 (C-3\`/C-5\`), 125.5 (C-5), 123.7 (C-4a), 119.4 (C-3), 62.4 (CH_2), 14.5 (CH_3).

Ethyl 2-*p*-tolylquinoline-4-carboxilate (65c)



Yield 65 % , brownish oil (lit. mp 54 ºC) (John *et al*., 1931)**.**

HRMS (ESI): calcd. for $C_{19}H_{18}NO_2$ $[M+H]^+$: 292.13375, found: 292.13321.

^{1}H NMR ($CDCl_3$): δ 8.73 (d, *J* = 8.5 Hz, 1H, H-5), 8.36 (s,1H, H-3), 8.21 (d, *J* = 8.5 Hz, 1H, H-8), 8.11 (d, *J* = 8.1 Hz, 2H, H-2\`/ H-6\`), 7.74 (dt, *J* = 8.3 Hz, *J* = 1.1 Hz, 1H, H-7), 7.58 (dt, *J* = 7.1 Hz, *J* = 1.3 Hz, 1H, H-6), 7.33 (d, *J* = 8.1 Hz, 2H, H-3\`/ H-5\`), 4.53 (q, *J* = 7.1 Hz, 2H, OCH_2CH_3), 2.42 (s, 3H, CH_3), 1.48 (t, *J* = 7.1 Hz, 3H, CH_3).

^{13}C NMR ($CDCl_3$): δ 166.6 (*C*OOEt), 156.7 (C-2), 149.3 (C-8a), 139.9 (C-1\`), 136.1(C-4), 136.0 (C-4\`), 130.3 (C-8), 129.8 (C-7), 129.7 (C-2\`/C-6\`), (127.6 C-3\`/C-5\`), 127.4 (C-6), 125.5 (C-5), 124.0 (C-4a), 120.1 (C-3), 61.9 (CH_2), 21.4 (CH_3), 14.4 (CH_2CH_3).

Ethyl 2-(4-fluorophenyl)quinoline-4-carboxylate (65d)



Yield; 61%, yellowish oil

HRMS (ESI): calcd. for $C_{18}H_{15}FNO_2$ $[M+H]^+$: 296.10868, found: 296.10901.

^{1}H NMR ($CDCl_3$): δ 8.71 (d , *J* = 8.5 Hz ,1H, H-5), 8.30 (s, 1H , H-3), 8.15-8.20 (m, 3H), 7.71-7.77 (m, *J* = 6.3 Hz, 1H, H-7), 7.57-7.62 (m, 1H, H-6), 7.20 (t, *J* = 8.7 Hz, 1H, H-3`/ H-5`), 4.52 (q, *J* = 7.1 Hz , 2H, CH_2), 1.48 (t, *J* = 7.1 Hz, 3H, CH_3).

^{13}C NMR ($CDCl_3$): δ 166.4 (*C*OOEt), 164.0 (d, $^1J_{C\text{-}F}$ = 248 Hz, C-4`), 155.6 (C-2), 149.2 (C-8a), 136.3 (C-4), 134.9 (d, $^4J_{C\text{-}F}$ = 2.9 Hz, C-1`), 130.5 (C-7), 130.1 (C-8), 129.4 (d, $^3J_{C\text{-}F}$ = 8.5 Hz, C-2`/C-6`), 127.9 (C-6), 125.4 (C-5), 123.9 (C-4a), 119.8 (C-3), 115.9 (d, $^2J_{C\text{-}F}$ = 21.5 Hz, C-3`/C-5`), 62.0 (CH_2), 14.4 (CH_3).

3.2.3. General procedure for preparation of (2-arylquinoline -4-yl)methanols (66a-d)

Ethyl 2-arylquinoline -4-carboxylate **(65a-d)** (2.1 mmol) were dissolved in ethanol (15 mL) and cooled to 0– 5 °C. Sodium borohydride (21 mmol) was added in fractions to the above solution under stirring in such a manner that the temperature of the reaction mixture did not rise above 10 °C. The reaction mixture was then refluxed for 3h at 80 °C. When the reaction was completed the hot mixture was filtered and cooled to recrystallize the product. The precipitated solid was filtered and air dried to get the desired compounds. Using this procedure, the following compounds were prepared:

(2-Phenylquinoline-4-yl) methanol (66a)

Yield; 80%, white solid, m.p = 130-132°C (lit. mp 102-104 ºC) (DasGupta *et al*., 2009).

HRMS (ESI): calcd. for $C_{16}H_{14}NO$ $[M+H]^+$: 236.10754, found: 236.10699.

^{1}H NMR ($CDCl_3$): δ 8.19 (d , *J* = 8.3 Hz,1H, H-5), 8.06 (dd, *J* = 8.2 Hz, *J* = 1.8 Hz, 2H, H-2\`/H-6\`), 7.89 (s, 1H, H-3), 7.85 (dd, *J* = 8.4 Hz, *J* = 0.9 Hz, 1H, H-8), 7.67-7.73 (m, 1H, H-7), 7.41-7.53 (m, 4H), 5.16 (s, 2H, CH_2), 1.24 (s, OH).

^{13}C NMR ($CDCl_3$): δ 157.4 (C-2) , 147.9 (C-4), 146.9 (C-8a), 139.4 (C-1\`), 130.1 (C-7), 129.6 (C-4\`), 129.5 (C-8), 128.8 (C-2\`/C-6\`), 127.6 (C-6), 126.5 (C-3\`/C-5\`), 124.7, (C-5), 122.7 (C-4a), 116.2 (C-3), 61.9 (CH_2).

(2-(4-Chlorophenyl)quinoline-4-yl)methanol (66b)

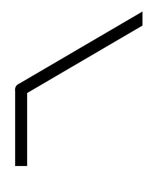
Yield; 73 %, white solid, m.p = 162-163 ºC.

HRMS (ESI): calcd. for $C_{16}H_{13}ClNO$ $[M+H]^+$: 270.06857, found: 270.06802.

^{1}H NMR (DMSO-d$_6$): δ 8.25 (d, *J* = 8.4 Hz, 2H, H-2`/ H-6`), 8.12 (s, 1H , H-3), 8.02-8.07 (m, 2H, H-5/H-8), 7.76 (d, *J* = 7.1 Hz, 1H, H-7), 7.59 (d, *J* = 8.4 Hz, 2H, H-3`/ H-5`), 7.58 (t, *J* = 8.4 Hz, 1H, H-6), 5.06 (s, 2H, CH_2), 3.32 (1H, OH).

^{13}C NMR (DMSO-d$_6$): δ 155.1 (C-2), 149.5 (C-4), 147.8 (C-8a), 138.1 (C-1`), 135.0 (C-4`), 130.2 (C-7), 130.2 (C-8), 129.4 (C-2`/C-6`), (129.3 (C-6), 127.0 C-3`/C-5`), 125.2 (C-5), 124.0 (C-4a), 115.6 (C-3), 60.4 (CH_2).

(2-*p*-Tolylquinoline-4-yl)methanol (66c)



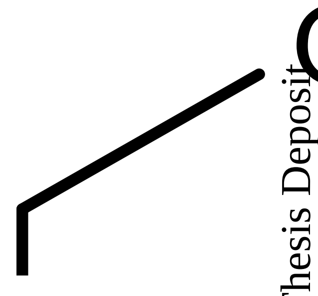
Yield ; 83% , yellowish amorphous solid.

HRMS (ESI): calcd. for $C_{17}H_{16}NO$ $[M+H]^+$: 250.12319, found: 250.12264.

^{1}H NMR (DMSO-d$_6$): δ 8.28 (d, *J* = 8.1 Hz, 2H, H-2`/ H-6`), 8.10 (s, 1H , H-3), 8.07 (dd, *J* = 8.2 Hz, *J* = 7.8 Hz, 2H), 7.76 (t, *J* = 7.2 Hz, 1H, H-7), 7.57 (d , *J* = 8.3 Hz, 2H, H-3`/ H-5`), 7.52 (t, *J* = 8.3 Hz , 1H, H-6), 5.14 (s, 2H , CH_2), 3.36 (1H, OH).

^{13}C NMR (DMSO-d$_6$): δ 151.6 (C-2), 147.6 (C-4), 142.8 (C-8a), 138.4 (C-1`), 135.8 (C-4`), 130.1 (C-7), 130.0 (C-8), 129.8 (C-2`/C-6`), 129.9 (C-6), 127.5 (C-3`/C-5`), 126.6 (C-5), 124.0 (C-4a), 115.6 (C-3), 57.0 (CH_2), 21.4 (CH_3).

(2-(4-Fluorophenyl)quinoline-4-yl)methanol (66d)



Yield; 88 %, white solid, m.p = 92 – 93 ºC.

HRMS (ESI): calcd. for $C_{16}H_{13}FNO$ $[M+H]^+$: 254.09812, found: 254.09757

^{1}H NMR (DMSO-d$_6$): δ 8.27 (dd, *J* = 8.9 Hz, *J* = 5.6 Hz, 2H, H-2`/ H-6`), 8.10 (s, 1H , H-3), 8.05 (d, *J* = 8.4 Hz, 1H, H-5), 8.02 (d, *J* = 8.2 Hz, 1H, H-8) 7.74 (dt, *J* = 8.4 Hz , *J* = 1.3 Hz, 1H, H-7), 7.56 (dt, *J* = 8.2 Hz , *J* = 1.3 Hz, 1H, H-6), 7.34 (d, *J* = 8.9 Hz, 2H, H-3`/ H-5`), 5.06 (s, 2H , CH_2OH), 3.38 (s, 1H, OH).

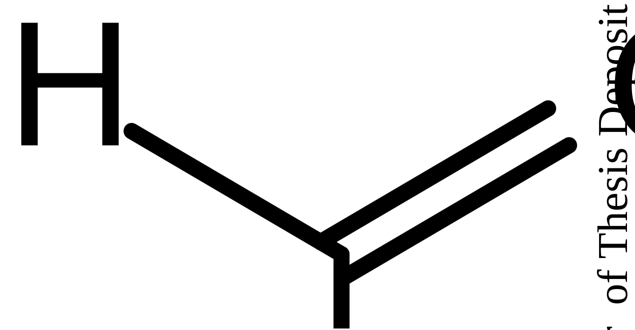
^{13}C NMR (DMSO-d$_6$): δ 163.7 (d, $^1J_{C\text{-}F}$ = 245 Hz, C-4`), 155.3 (C-2), 149.4 (C-8a), 147.8 (C-4), 135.9 (d, $^4J_{C\text{-}F}$ = 2.9 Hz, C-1`), 130.1 (C-7), 130.1 (C-8), 129.8 (d, $^3J_{C\text{-}F}$ = 8.5 Hz, C-2`/C-6`), 126.8 (C-6), 125.1 (C-4a), 124.0 (C-5), 116.3 (d, $^2J_{C\text{-}F}$ = 21.5 Hz, C-3`/C-5`), 115.6 (C-3), 60.4 (CH_2OH).

3.2.4. General procedure for preparation of 2-aryl-quinoline-4-carboxaldehydes (67a-d)

The 2-aryl-quiniline-4-yl)methanol (**66a-d**) (0.051 mol) was dissolved in dry dioxane (200 mL), and SeO_2 (0.025 mol) was added. The solution was heated at reflux for 2.5 h, filtered while hot, and evaporated to dryness. The crude residue was purified by column chromatography (SiO_2, $CHCl_3$) to give 2-aryl-quinoline-4-carboxaldehyde (**67a-d**) as a solid material.

Using the same general procedure, the following compounds were prepared:

2-Phenylquinoline-4-carboxaldehyde (67a)



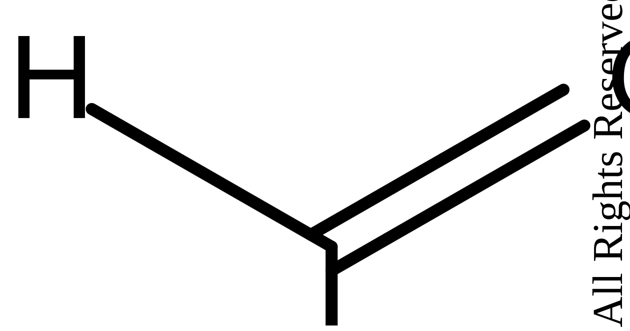
Yield; 70%, yellowish solid, m.p = 70-71 °C (lit. m.p 75 ºC) (Tarbell *et al*., 1945).

HRMS (ESI): calcd. for $C_{16}H_{12}NO$ $[M+H]^+$: 234.09189, found: 234.09134 .

^{1}H NMR (DMSO-d$_6$): 10.54 (s, 1H, C*H*O), 8.94 (d , *J* = 8.5 Hz, 1H, H-5), 8.71 (s, 1H, H-3), 8.34 (d, *J* = 7.8 Hz, 2H, H-2`/ H-6`), 8.19 (d, *J* = 8.4 Hz, 1H, H-8), 7.87 (d, *J* = 7.0 Hz, 1H, H-7), 7.76 (dd, *J* = 8.3 Hz, *J* = 7.1 Hz, 1H, H-6), 7.51-7.61 (m, 3H, H-3`/ H-4`/H-5`).

^{13}C NMR (DMSO-d$_6$): 195.4 (C*H*O), 157.1 (C-2), 149.0 (C-8a), 138.6 (C-4), 138.2 (C-1`), 131.0 (C-7), 130.7 (C-4`), 130.2 (C-8), 129.6 (C-2`/C-6`), 129.4 (C-6), 127.7 (C-3`/C-5`), 125.0 (C-5), 124.8 (C-4a), 122.8 (C-3).

2-(4-Chlorophenyl)quinoline-4-carbaldehyde (67b)



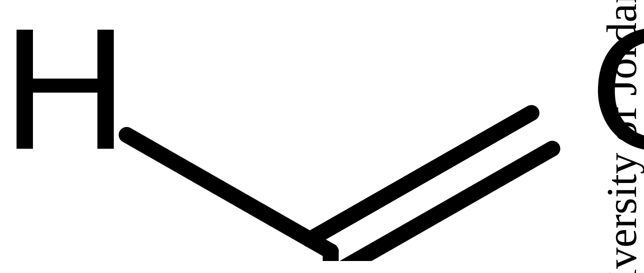
Yield; 61%, yellowish solid, m.p = 130-131 ºC .

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^{1}H NMR ($CDCl_3$): δ 10.54 (s, 1H , C*H*O), 8.94 (dd , *J* = 7.8 Hz, *J* = 0.6 Hz, 1H, H-5), 8.22 (dd, *J* = 8.0 Hz, *J* = 0.5 Hz, 1H, H-8), 8.12-8.16 (m, 3H), 7.77-7.82 (m,1H, H-7), 7.64 -7.69 (m, 1H, H-6), 7.47-7.51 (m, 2H, H-3`/ H-5`).

^{13}C NMR ($CDCl_3$): δ *δ* 192.8 (*C*HO), 156.0 (C-2), 149.4 (C-8a), 137.8 (C-4), 136.8 (C-1`), 136.4 (C-4`), 130.5 (C-7), 130.3(C-8), 129.3 (C-2`/C-6`), 129.1(C-6), 128.7 (C-3`/C-5`), 124.2 (C-5), 123.3 (C-4a), 123.0 (C-3).

2-*p*-Tolylquinoline-4-carbaldehyde (67c)



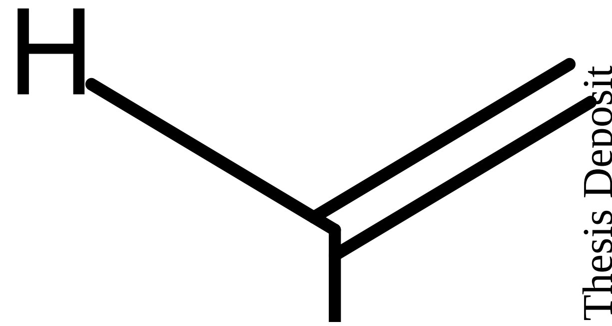
Yield; 67%, yellowish, amorphous solid.

HRMS (ESI): calcd. for $C_{17}H_{14}NO$ $[M+H]^+$ 248.10754, found 248.10699.

^{1}H NMR (,$CDCl_3$): δ 10.55 (s, 1H, CHO), 8.96 (d , *J* = 8.41 Hz, 1H ,H-5), 8.23 (d, *J* = 8.3 Hz, 1H, H-8), 8.22 (s, 1H), 8.12 (d, *J* = 8.1 Hz, 2H, H-2`/H-6`),7.79 (dt, *J* = 7.0 Hz, *J* = 1.4 Hz,1H,H-7), 7.63-7.69 (m,1H,H-6), 7.35 (d, *J* = 8.1 Hz, 2H, H-3`/H-5`), 2.43 (s, CH_3).

^{13}C NMR ($CDCl_3$): δ 193.2 (*C*HO), 157.4 (C-2), 149.4 (C-8a), 140.3 (C-4), 137.6 (C-1`), 135.7 (C-4`), 130.3 (C-8), 130.2 (C-7) , 129.9 (C2`/C6`), 128.7 (C-6),127.3 (C3`/C5`), 124.2 (C-5), 124.2 (C-4a), 122.8 (C-3), 21.5 (CH_3) .

2-(4-Fluorophenyl)quinoline-4-carbaldehyde (67d)



Yield; 70.6 %, yellowish solid, m.p = 118 – 119 ºC.

^{1}H NMR (DMSO-d$_6$): δ 10.51 (s, 1H , C*H*O), 8.90 (d , *J* = 8.4 Hz, 1H, H-5), 8.66 (s, 1H, H-3), 8.36 (dd, *J* = 8.8 Hz, *J*= 5.6 Hz, 1H, H-2`/ H-6`), 8.14 (d, *J* = 8.4 Hz, 1H, H-8), 7.84 (dd, *J* = 8.2 Hz, *J* = 7.0 Hz,1H, H-7), 7.72 (dd, *J* = 8.3 Hz, *J* = 7.2 Hz,1H, H-6), 7.39 (t, *J* = 8.8 Hz, 2H, H-3`/ H-5`).

^{13}C NMR (DMSO-d$_6$): δ 195.3 (*C*HO), 164.1 (d, $^1J_{C-F}$ = 246 Hz, C-4`), 156.0 (C-2), 148.9 (C-8a), 138.3 (C-4), 134.6 (d, $^4J_{C-F}$ = 2.9 Hz, C-1`), 131.0 (C-7), 130.1 (C-8), 130.0 (d, $^3J_{C-F}$ = 8.7 Hz, C-2`/C-6`), 129.4 (C-6), 124.9 (C-5), 124.7 (C-3), 122.7 (C-4a), 116.5 (d, $^2J_{C-F}$ = 21.5 Hz, C-3`/C-5`).

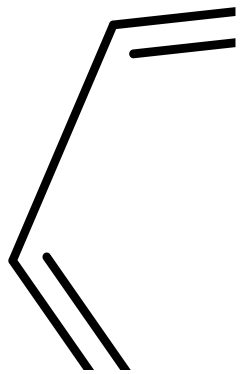
3.2.5. General procedure for preparation of the imidazole derivatives (69a-j, 70a-j, 71a-j and 72a-j)

1,2-Diketone (Benzil derivative) (0.5 mmol), 2-aryl-quinoline-4-carbaldehyde (**67a-d**) (1 eq), and ammonium acetate (20 mmol) were combined and dissolved in 7.0 mL of AcOH in a 10 mL Biotage Initiator reaction vial containing a magnatic ring stir bar. The reaction vessel was heated in the Biotage Initiator reactor cavity for 12 min at 130 ºC, after which the vessel was rapidly cooled to 40 ºC by the unit. The reaction mixture was added

dropwise to a 0 ºC concentrated ammonia solution and immediately formed a precipitate which was collected by filtration and washed with H_2O. The solid was dried and recrystallized from ethanol.

Using the same general procedure, the following compounds were prepared:

4-(4,5-Diphenyl-1*H*-imidazol-2-yl)-2-phenylquinoline (69a)



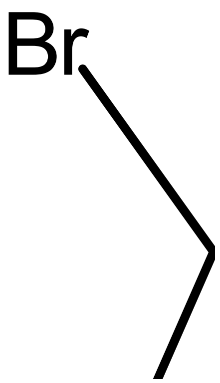
Yield; 96%, pale yellow solid, m. p = 342-344 ºC.

HRMS (ESI): calcd. for $C_{30}H_{20}N_3$ $[M-H]^-$: 422.16572, found: 422.16853.

^{1}H NMR (DMSO-d$_6$): δ 13.25 (s, NH), 9.60 (d, *J* = 7.6 Hz, 1H, H-5), 8.59 (s, 1H, H-3), 8.38 (d, *J* = 6.9 Hz, 2H, H-2`/H-6`), 8.11 (d, *J* = 7.9 Hz, 1H, H-8), 7.82 (brt, 1H, H-7), 7.64 (brt, 1H, H-6), 7.25-7.64 (m, 13H).

^{13}C NMR (DMSO-d$_6$): δ 156.2, 149.3, 144.1, 139.1, 138.7, 135.3, 131.2, 130.4, 130.3, 130.1, 129.8, 129.3, 129.3, 128.9, 128.8, 127.8, 127.7, 127.6, 127.5, 127.4, 124.1, 117.1.

4-(4-5-Bis(4-bromophenyl)-1*H*-imidazol-2-yl)-2-phenylquinoline (69b)



Yield; 95 %, offwhite solid, m. p = 284 ºC.

HRMS (ESI): calcd. for $C_{30}H_{20}Br_2N_3$ $[M-H]^-$: 580.00240, found: 580.00185.

^{1}H NMR (DMSO-d$_6$): δ 13.33 (s, NH), 9.49 (d, *J* = 8.2 Hz, 1H, H-5), 8.56 (s, 1H, H-3), 8.36 (d, *J* =7.1 Hz, 2H, H-2`/H-6`), 8.11 (d, *J* = 8.2 Hz, 1H, H-8), 7.81 (t, *J* = 7.1 Hz, 1H, H-7), 7.49-7.70 (m, 12H).

^{13}C NMR (DMSO-d$_6$): δ 156.2, 149.2, 144.7, 140.0, 135.2, 132.2, 131.1, 130.5, 130.3, 130.2, 129.3, 127.8, 127.6, 127.5, 124.0, 117.4.

4-(4-5-Bis(4-fluorophenyl)-1*H*-imidazol-2-yl)-2-phenylquinoline (69c)

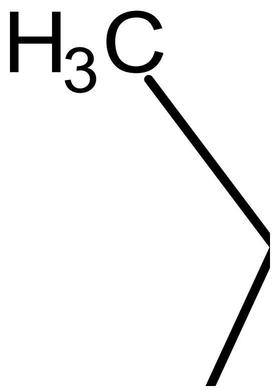
Yield; 93 %, white solid, m. p = 338 ºC.

HRMS (ESI): calcd. for $C_{30}H_{20}F_2N_3$ $[M+H]^+$: 460.16253, found: 460.16198.

^{1}H NMR (DMSO-d$_6$): δ 13.30 (s, 1H, NH), 9.56 (d, *J* = 8.4 Hz, 1H, H-5), 8.57 (s, 1H, H-3), 8.37(d, *J* = 7.2 Hz, 2H, H-2`/H-6`), 8.10 (d, *J* = 8.2 Hz, 1H, H-8), 7.80 (t, *J* = 7.5 Hz, 1H, H-7), 7.20-7.70 (m, 12H).

^{13}C NMR (DMSO-d$_6$): δ 156.2, 149.3, 144.1, 139.0, 135.2, 131.5, 130.4, 130.3, 130.1, 129.3, 127.8, 127.6, 124.0, 117.1, 116.6, 116.3, 116.1, 115.8.

4-(4,5-Di-*p*-tolyl-1*H*-imidazol-2-yl)-2-*p*-tolylquinoline (69d)



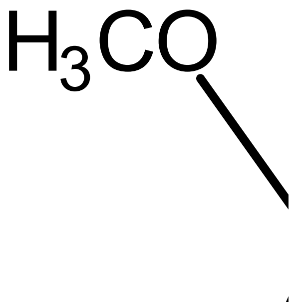
Yield; 99 %, orange solid, m. p = 275 ºC.

HRMS (ESI): calcd. for $C_{32}H_{26}N_3$ $[M+H]^+$: 452.21267, found: 452.21212.

^{1}H NMR (DMSO-d$_6$): δ 13.14 (s, NH), 9.60 (d, *J* = 8.4 Hz, 1H , H-5), 8.57 (s, 1H, H-3), 8.37 (d, *J* = 8.4 Hz, 2H, H-2`/H-6`), 8.10 (d, *J* = 8.3 Hz, 1H, H-8), 7.80 (dt, *J* = 6.8 Hz, *J* = 1.4 Hz, 1H, H-7), 7.67 (dt, *J* = 8.3 Hz, *J* = 1.4 Hz, 1H, H-6), 7.45-7.60 (m, 7H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 2.35 (s, 3H), 2.29 (s, 3H).

^{13}C NMR (DMSO-d$_6$): δ 156.2 , 149.3, 143.8, 139.1, 138.6, 138.1, 136.5, 135.4, 132.5, 130.3, 130.2, 130.1, 129.8, 129.4, 129.3, 129.0, 128.3, 127.8, 127.6, 127.4, 124.1, 117.0, 21.4, 21.3 .

4-(4,5-Di-*p*-tolyl-1*H*-imidazol-2-yl)-2-phenylquinoline (69e)



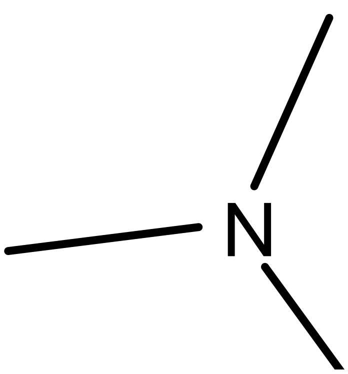
Yield; 97 %, reddish solid, m. p = 140 ºC.

HRMS (ESI): calcd. for $C_{32}H_{26}N_3O_2$ $[M+H]^+$: 484.20250, found: 484.20195.

¹H NMR (DMSO-d₆): δ 13.09 (s, NH), 9.63 (d, *J* = 8.5 Hz, 1H, H-5), 8.57 (s, 1H, H-3), 8.37 (d, *J* = 7.9 Hz, 2H, H-2`/H-6`), 8.09 (d, *J* = .4 Hz, 1H, H-8), 7.79 (t, *J* = 6.9 Hz, 1H, H-7), 7.66 (t, *J* = 8.2 Hz, 1H, H-6), 7.57-7.60 (m, 7H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3).

¹³C NMR (DMSO-d₆): δ 159.7, 158.7, 156.2, 149.3, 143.4, 139.1, 138.2, 135.3, 130.6, 130.3, 130.2, 130.1, 129.3, 128.9, 128.7, 127.8, 127.4, 124.1, 123.5, 116.8, 114.8, 114.3, 55.8, 55.6.

4,4`-(2-(2-Phenylquinolin-4-yl)-1*H*-imidazole-4,5-diyl)bis(N,N-dimethylaniline) (69f)



Yield; 93 %, brownish solid, m. p = 119-121 ºC.

HRMS (ESI): calcd. for $C_{34}H_{32}N_5$ $[M+H]^+$: 510.26577, found: 510.26522.

^{1}H NMR (DMSO-d$_6$): δ 9.60 (d, *J* = 8.3 Hz, 1H, H-5), 8.59 (s, 1H, H-3), 8.38 (d, *J* = 7.3 Hz, 2H, H-2\`/H-6\`), 8.11 (d, *J* = 8.3 Hz, 1H, H-8), 7.81(t, *J* = 7.5 Hz, 1H, H-7), 7.67 (t, *J* = 7.5 Hz, 1H, H-6), 7.53-7.60 (m, 3H), 7.44 (d, *J* = 8.2 Hz, 4H), 6.76(d, *J* = 8.2 Hz, 2H), 2.96 (brs, 12H, phenyl-N-(CH_3)$_2$).

4-(4-5-Di(pyridin-2-yl)-1*H*-imidazol-2-yl)-2-phenylquinoline (69g)

Yield; 95 %, yellowish solid, m. p = 184-187 ºC.

HRMS (ESI): calcd. for $C_{28}H_{20}N_5$ $[M+H]^+$: 426.17187, found: 426.17132 .

^{1}H NMR (DMSO-d$_6$): δ 9.33 (d, *J* = 8.3 Hz, 1H, H-5), 8.80 (d, *J* = 3.8 Hz, 2H, H-2\`/H6\`), 8.68 (s, 1H, H-3), 8.37 – 8.42 (m, 4H), 8.02 – 8.09 (m, 3H), 7.76(t, *J* = 6.9 Hz, 1H, H-7), 7.63(t, *J* = 8.2 Hz, 1H, H-6), 7.53 – 7.58 (m, 5H) .

^{13}C NMR (DMSO-d$_6$): δ 172.5, 156.1, 149.0, 147.4, 147.1, 145.7, 139.6, 138.9, 134.4, 130.3, 130.3, 130.1, 129.2, 128.0, 127.7, 127.2, 124.0, 123.9, 118.7

4-(4,5-Di(thiophen-2-yl)-1*H*-imidazol-2-yl)-2-phenylquinoline (69h)

Yield; 95 %, yellow solid, m. p = 322-323 ºC.

HRMS (ESI): calcd. for $C_{26}H_{18}N_3S_2$ $[M+H]^+$: 436.09421, found: 436.09367 .

^{1}H NMR (DMSO-d$_6$): δ 13.47 (s, 1H. NH), 9.50 (d, *J* = 8.5 Hz, 1H, H-5), 8.65 (s, 1H, H-3), 8.37 (d, *J* = 7.0 Hz, 2H, H-2`/ H-6`,), 8.12 (d, *J* = 8.2 Hz, 1H, H-8), 7.78-7.84 (m, 1H. H-7),7.66-7.71 (m, 1H, H-6), 7.05-7.79 (m, 9H).

^{13}C NMR (DMSO-d$_6$): δ 156.2, 149.3, 144.3, 138.9, 134.7, 130.5, 130.3, 130.2, 129.3, 128.1, 127.8, 127.6, 127.4, 125.8, 124.0, 117.3.

2-(2-Phenylquinolin-4-yl)-*H*-phenanthro[9,10-d]imidazole (69i)

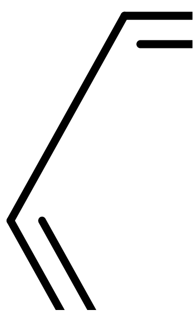
Yield; 93 %, offwhite solid, m.p = 249-250 ºC.

HRMS (ESI): calcd. For $C_{30}H_{20}N_3$ $[M+H]^+$: 422.16572, found: 422.16517 .

^{1}H NMR (DMSO-d_6): δ 13.91 (s, 1H, NH), 9.60 (d, *J* = 7.8 Hz, 1H, H-5), 8.87 (brs, 2H), 8.67-8.73 (m, 2H), 8.57-8.59 (m, 1H), 8.42 (d, *J* = 9.0 Hz, 2H, H-2`/H-6`), 8.18 (d, *J* = 6.0 Hz, 1H, H-8), 7.86 (t, *J* = 6.0 Hz, 1H, H-7), 7.52-7.74 (m, 8H).

^{13}C NMR (DMSO-d_6): δ 156.3, 149.3, 147.4, 139.0, 138.1, 136.0, 130.6, 130.4, 130.3, 129.5, 128.7, 128.3, 127.9, 127.7, 127.6, 126.6, 126.1, 124.8, 124.4, 122.9, 118.5.

2-(2-Phenylquinolin-4-yl)-1*H*-imidazo[4,5-*f*][1,10]phenanthroline (69j)



Yield; 94%, red amorphous solid.

^{1}H NMR (DMSO-d_6): δ 13.93 (s, 1H, NH), 9.60 (d, *J* = 8.3 Hz, 1H, H-5), 8.89 (brd, *J* = 6.6 Hz, 2H), 8.74 (s, 1H, H-3), 8.42 (d, *J* = 7.1 Hz, 2H, H-2`/ H-6`), 8.18 (d, *J* = 7.9 Hz, 1H, H-8), 7.87 (t, *J* = 7.1 Hz, 1H, H-7), 7.77 (t, *J* = 7.8 Hz, 2H,), 7.55-7.70 (m, 6H).

2-(4-Chlorophenyl)-4-(4,5-diphenyl-1*H*-imidazol-2-yl)quinoline (70a)

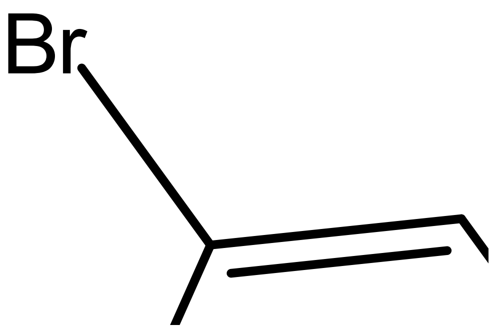
Yield; 91 %, orange solid, m. p = 240-242 ºC.

HRMS (ESI): calcd. for $C_{30}H_{19}ClN_3$ $[M-H]^-$: 456.12675, found: 456.12730.

^{1}H NMR (DMSO-d$_6$): δ 13.27 (s, NH), 9.63 (d, *J* = 7.9 Hz, 1H, H-5), 8.59 (s, 1H, H-3), 8.40 (d, *J* = 8.6 Hz, 2H, H-2\`/ H-6\`), 8.10 (d, *J* = 8.2 Hz, 1H, H-8), 7.81 (dt, *J* = 8.2 Hz, *J* = 1.3 Hz, 1H, H-7), 7.25-7.72 (m, 13H).

^{13}C NMR (DMSO-d$_6$): δ 154.9, 149.2, 144.0, 138.7, 137.8, 135.4, 135.2, 131.1, 130.5, 130.1, 129.9, 129.5, 129.4, 129.3, 128.9, 127.7, 127.6, 127.4, 124.1, 116.8.

4-(4,5-Bis(4-bromophenyl)-1*H*-imidazol-2-yl)-2-(4-chlorophenyl)quinoline (70b)



Yield; 94%, white solid, m.p = 325-326 ºC.

HRMS (ESI): calcd. for $C_{30}H_{19}Br_2ClN_3$ $[M+H]^+$: 613.96343, found:613.95140 .

^{1}H NMR (DMSO-d$_6$): δ 13.34 (s, 1H, NH), 9.50 (d, *J* = 6.0 Hz, 1H, H-5), 8.56 (s, 1H, H-3), 8.39 (d, *J* = 9.0 Hz, 2H, H-2\`/ H-6\`), 8.10 (d, *J* = 6.0 Hz, 1H, H-8), 7.81 (psudo triplet, *J* = 6.0 Hz, 1H, H-7), 7.62-7.71 (m, 6H), 7.52-7.54 (m, 5H).

^{13}C NMR (DMSO-d$_6$): δ 154.9, 149.2, 144.5, 137.7, 135.3, 132.3, 131.1, 130.6, 130.1, 129.8, 129.5, 129.4, 127.8, 127.5, 124.1, 117.1.

4-(4,5-Bis(4-fuorophenyl)-*H*-imidazol-2-yl)-2-(4-chlorophenyl)quinoline (70c)

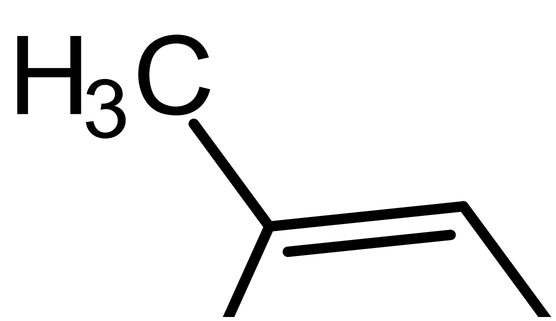
Yield; 95%, white solid, m.p = 278-279 ºC.

HRMS (ESI): calcd. for $C_{30}H_{19}ClF_2N_3$ $[M+H]^+$: 494.12356, found: 494.12301 .

^{1}H NMR (DMSO-d$_6$): δ 13.29 (s, 1H, NH), 9.57 (d, *J* = 8.4 Hz, 1H, H-5), 8.57 (s, 1H, H-3), 8.39 (d, *J* = 8.5 Hz, 2H, H-2`/ H-6`), 8.10 (d, *J* = 8.3 Hz , 1H, H-8), 7.81 (dd, *J* = 8.0 Hz, *J* = 8.0 Hz, 1H, H-7), 7.69 (t, *J* = 8.5 Hz, 1H, H-6), 7.59-7.66 (m, 6H).

^{13}C NMR (DMSO-d$_6$): δ 154.9, 149.2, 144.0, 137.8, 135.4, 135.2, 131.5, 130.5, 130.1, 129.5, 129.4, 127.8, 127.6, 124.1, 116.8, 116.1 .

2-(4-Chlorophenyl)-4-(4,5-di-*p*-tolyl-1*H*-imidazol-2-yl)quinoline (70d)



Yield; 98%, white solid, m.p = 283-284 ºC.

HRMS (ESI): calcd. for $C_{32}H_{23}ClN_3$ $[M-H]^-$: 484.15805, found: 484.15860 .

^{1}H NMR (DMSO-d$_6$): δ 9.61 (d, *J* = 6.0 Hz, 1H , H-5), 8.56 (s, 1H, H-3), 8.40 (d, *J* = 9.0 Hz, 2H, H-2`/ H-6`), 8.09 (d, *J* = 8.2 Hz, 1H, H-8), 7.79 (t, *J* = 9.0 Hz, 1H, H-7), 7.46 – 7.70 (m, 11H), 2.46 (s,3H, CH_3), 2.31 (s, 3H, CH_3).

^{13}C NMR (DMSO-d$_6$): δ 154.9, 149.2, 143.7, 137.9, 135.5, 135.2, 130.5, 130.1, 129.7, 129.5, 129.4, 127.8, 127.6, 124.1, 116.7, 21.4.

4-(4,5-Bis(4-methoxyphenyl)-1*H*-imidazol-2-yl)-2-(4-chlorophenyl)quinoline (70e)

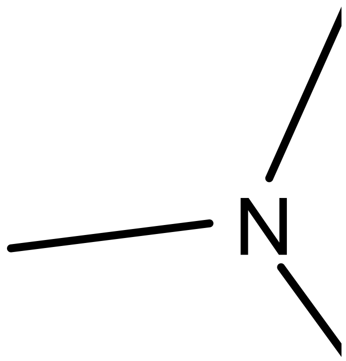
Yield; 96%, reddish solid, m.p = 110-112 ºC.

HRMS (ESI): calcd. for $C_{32}H_{25}ClN_3O_2$ [M+H]$^+$: 518.16353, found: 518.16298 .

^{1}H NMR (DMSO-d$_6$): δ 13.12 (s, 1H, NH), 9.66 (d, *J* = 8.4 Hz, 1H, H-5), 8.57 (s, 1H, H-3), 8.40 (d, *J* = 8.4 Hz, 2H, H-2`/ H-6`), 8.08 (d, *J* = 8.3 Hz, 1H, H-8), 7.67 (t, *J* = 6.7 Hz, 1H, H-7), 7.63 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 3.88 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3).

^{13}C NMR (DMSO-d$_6$): 159.7, 158.7, 154.8, 149.2, 143.4, 138.2, 137.9, 135.4, 135.2, 130.5, 130.4, 130.1, 129.5, 129.4, 128.9, 128.7, 127.8, 127.6, 124.1, 123.4, 116.4, 114.8, 114.3, 55.7, 55.5.

4,4`-(2-(2-(4-Chlorophenyl)quinolin-4-yl)-1*H*-imidazole-4,5-diyl)bis(N,N-dimethylaniline) (70f)



Yield; 95%, brownish solid, m.p = 119-121 ºC.

HRMS (ESI): calcd. for $C_{34}H_{30}ClN_5$ $[M]^+$: 543.21897, found: 543.21843.

^{1}H NMR (DMSO-d$_6$): δ 9.61(d, *J* = 6.9 Hz, 1H, H-5), 8.58 (s, 1H, H-3), 8.41 (d, *J* = 8.2 Hz, 2H, H-2`/H-6`), 8.09 (d, *J* = 8.2 Hz, 1H, H-8), 7.79 (dd, *J* = 7.7 Hz, 1H, H-7), 7.59-7.69 (m, 3H), 7.44 (d, *J* = 8.1 Hz, 4H), 6.75 (d, *J* = 8.3 Hz, 2H), 2.90 (brs, 12H, phenyl-N-($CH_3)_2$).

2-(4-Chlorophenyl)-4-(4,5-di(pyridin-2-yl)-1*H*-imidazol-2-yl)quinoline (70g)

Yield; 93%, yellow solid, m.p = 78-80 ºC.

HRMS (ESI): calcd. for $C_{28}H_{19}ClN_5$ $[M+H]^+$: 460.13290, found: 460.13235.

¹H NMR (DMSO-d$_6$): δ 13.70 (s, 1H, NH), 9.53 (d, *J* = 8.4 Hz, 1H, H-5), 8.70 (s, 1H, H-3), 8.46 (d, *J* = 8.5 Hz, 2H, H-2`/ H-6`), 7.03-8.34 (m, 13H).

¹³C NMR (DMSO-d$_6$): δ 154.9, 149.1, 137.9, 135.2, 130.5, 130.2, 129.6, 129.5, 129.3, 127.8, 127.6, 123.2, 117.9.

2-(4-Chlorophenyl)-4-(4,5-di(thiophen-2-yl)-1*H*-imidazol-2-yl)quinoline (70h)

Yield; 93 %, yellow Solid, m. p = 280-282 ºC.

HRMS (ESI): calcd. for $C_{26}H_{27}ClN_3S_2$ $[M-H]^-$: 469.04742, found: 472.16197.

¹H NMR (DMSO-d$_6$): δ 13.44 (s, 1H, NH), 9.81 (d, *J* = 9.0 Hz, 1H, H-5), 8.56 (s, 1H, H-3), 8.39 (d, *J* = 9.0 Hz, 2H, H-2`/ H-6`), 8.11 (d, *J* = 9.0 Hz, 1H, H-8), 7.81 (d, *J* = 9.0 Hz, 1H, H-7), 7.45-7.71 (m, 2H), 7.64 (d, *J* = 9.0 Hz, 4H), 7.53 (d, *J* = 6.0 Hz, 4H).

¹³C NMR (DMSO-d$_6$): δ 154.9, 149.2, 144.5, 137.7, 135.3, 132.3, 131.1, 130.6, 130.1, 129.8, 129.5, 129.4, 127.8, 127.5, 124.1, 117.1.

2-(2-(4-Chlorophenyl)quinolin-4-yl)-1*H*-phenanthro[9,10-*d*]imidazole (70i)

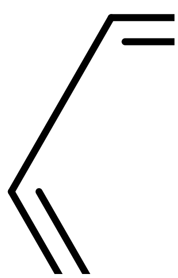
Yield; 95 %, brown solid, m. p = 280ºC.

HRMS (ESI): calcd. For $C_{26}H_{27}ClN_3S_2$ $[M-H]^-$: 456.12675, found: 456.12620 .

^{1}H NMR (DMSO-d$_6$): δ 13.90 (s, NH), 9.60 (d, *J* = 8.1 Hz, 1H, H-5), 8.87 (d, *J* = 8.2 Hz, 2H), 8.72 (s, 1H, H-3), 8.62 (brs, 2H), 8.44 (d, *J* = 8.6 Hz, 2H, H-2`/H-6`), 8.17 (d, *J* = 8.2 Hz, 1H, H-8), 7.86 (t, *J* = 6.9 Hz, 1H, H-7), 7.64-7.79 (m, 5H).

^{13}C NMR (DMSO-d$_6$): δ 155.0, 149.2, 147.3, 137.7, 136.1, 135.3, 130.7, 130.2, 129.6, 129.5, 128.1, 127.8, 127.6, 126.3, 124.5, 122.7, 118.2.

2-**(2-(4-Chlorophenyl)quinolin-4-yl)-1*H*- imidazo[4,5-*f*][1,10]phenanthroline (70j)**



Yield; 93 %, brown solid, m.p = 302 ºC.

HRMS (ESI): calcd. for $C_{30}H_{19}ClN_3O_2$ $[M+H]^+$: 518.16353, found: 518.16298 .

^{1}H NMR (DMSO-d$_6$): δ 9.54 (d, *J*=8.5 Hz, 1H, H-5), 8.99-9.05 (m, 4H), 8.80 (s, 1H, H-3), 8.47 (d, *J* = 8.5 Hz, 2H, H-2\`/ H-6\`), 8.16 (d, *J* = 8.1 Hz, 1H, H-8), 7.83-7.89 (m, 3H), 7.75(dd, *J* = 7.6 Hz, 1H, H-6), 7.66 (d, *J* = 8.5 Hz, 2H).

^{13}C NMR (DMSO-d$_6$): δ 155.0, 149.2, 148.8, 144.4, 137.6, 135.3, 130.8, 130.6, 130.2, 129.6, 129.5, 128.2, 127.5, 124.4, 124.0, 118.6.

4-(4,5-Diphenyl-1*H*-imidazol-2-yl)-2-*p*-tolylquinoline (71a)

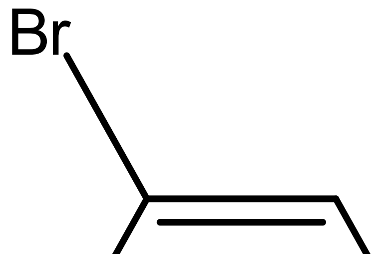
Yield; 93 %, yellow solid, m.p = 275 ºC.

HRMS (ESI): calcd. for $C_{31}H_{24}ClN_3$ $[M+H]^+$: 438.19702, found: 438.19647 .

^{1}H NMR (DMSO-d$_6$): δ 13.27 (s, NH), 9.58 (d, *J* = 8.6 Hz, 1H, H-5), 8.56 (s, 1H, H-3), 8.29 (d, *J* = 8.1 Hz, 2H, H-2\`/H-6\`), 8.09 (d, *J* = 8.5 Hz, 1H, H-8),7.11-7.84 (m, 14H), 2.39 (s, 3H, C*H*$_3$).

^{13}C NMR (DMSO-d$_6$): δ 156.1, 149.3, 144.1, 140.0, 138.6, 136.2, 135.2, 135.2, 131.2, 130.3, 130.0, 129.9, 129.8, 129.3, 129.3, 128.9, 128.8, 127.7, 127.6, 127.4, 127.3, 124.0, 116.8, 21.5 .

4-(4,5-Bis(4-bromophenyl)-1*H*-imidazol-2-yl)-2-*p*-tolylquinoline (71b)



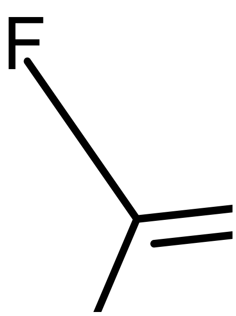
Yield; 93%, white solid, m.p = 296 ºC.

HRMS (ESI): calcd. for $C_{31}H_{21}Br_2N_3$ $[M+H]^+$: 594.01805, found: 596.01281.

^{1}H NMR (DMSO-d$_6$): δ 13.33 (s, NH), 9.46 (d, *J* = 8.0 Hz, 1H, H-5), 8.54 (s, 1H, H-3), 8.28 (d, *J* = 8.1 Hz, 2H, H-2`/H-6`), 8.09 (d, *J* = 8.0 Hz, 1H, H-8), 7.79 (t, *J* = 7.1 Hz, 1H, H-7), 7.70 (d, *J* = 8.5 Hz, 2H, H-3`/H-5`), 7.65 (t, *J* = 7.1 Hz, 1H, H-6), 7.55 (brs, 4H), 7.54 (d, *J* = 10.5 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 2.39 (s, 3H, C*H*$_3$).

^{13}C NMR (DMSO-d$_6$): δ 156.1, 149.2, 144.7, 140.0, 137.8, 136.2, 135.1, 134.2, 132.4, 132.0, 131.2, 130.4, 130.0, 129.9, 129.7, 127.7, 127.4, 123.9, 122.2, 120.7, 117.1, 21.4.

4-(4,5-Bis(4-fluorophenyl)-1*H*-imidazol-2-yl)-2-*p*-tolylquinoline (71c)



Yield; 93%, White solid, m. p = 279 ºC.

HRMS (ESI): calcd. for $C_{31}H_{22}F_2N_3$ $[M+H]^+$: 474.17818, found: 474.17763 .

¹H NMR (DMSO-d$_6$): δ 13.27 (s, NH), 9.53 (d, *J* = 6.0 Hz, 1H, H-5), 8.54 (s, 1H, H-3), 8.28 (d, *J* = 9.0 Hz, 1H, H-8), 8.09 (d, *J* = 9.0 Hz,2H, H-2`/H-6`), 7.78 (t, *J* = 9.0 Hz, 1H, H-7), 7.59-7.67 (m, 5H), 7.31-7.39 (m, 4H), 7.16-7.21 (m, 2H), 2.38 (s, 3H, CH_3).

¹³C NMR (DMSO-d$_6$): δ 156.1, 149.3, 144.1, 140.0, 136.2, 135.1, 131.6, 131.4, 130.4, 130.0, 129.9, 129.54, 129.4, 127.7, 127.6, 127.3, 124.0, 116.9, 116.6, 116.3, 116.0, 115.7, 21.5.

4-(4,5-Di-*p*-tolyl-1*H*-imidazol-2-yl)-2-*p*-tolylquinoline (71d)

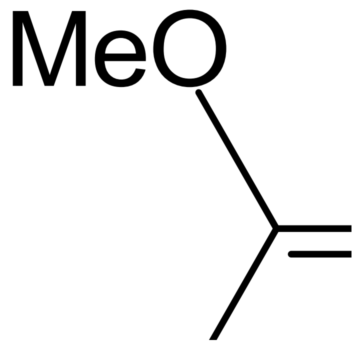
Yield; 98%, orange solid, m. p = 288 ºC.

HRMS (ESI): calcd. for $C_{33}H_{28}N_3$ $[M+H]^+$: 466.22832, found: 466.22777.

¹H NMR (DMSO-d$_6$): 13.14 (s, NH), 9.57 (d, *J* = 8.0 Hz, 1H, H-5), 8.54 (s, 1H, H-3), 8.28 (d, *J* = 8.2 Hz, 2H, H-2`/ H-6`), 8.10 (d, *J* = 8.2 Hz, 1H, H-8), 7.78 (dt, *J* = 8.1 Hz, *J* = 1.2 Hz, 1H, H-7), 7.67 (dd, *J* = 8.2 Hz, *J* = 1.0 Hz, 1H, H-6), 7.50 (d, *J* = 8.1 Hz, 2H), 7.45-7.51 (m, 4H), 7.37 (d, *J* = 8.1 Hz, 2H, H-3`/H-5`), 7.28 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 2.38 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.28 (s, 3H, CH_3).

¹³C NMR (DMSO-d$_6$): 156.1, 149.3, 143.8, 139.9, 138.5, 138.1, 136.4, 136.3, 135.3, 132.5, 130.3, 130.0, 129.9, 129.8, 129.4, 129.0, 128.3, 127.7, 127.6, 127.6, 127.2,124.0, 116.7, 21.4, 21.4, 21.3.

4-(4,5-Bis(4-methoxyphenyl)-1*H*-imidazol-2-yl)-2-*p*-tolylquinoline (71e)



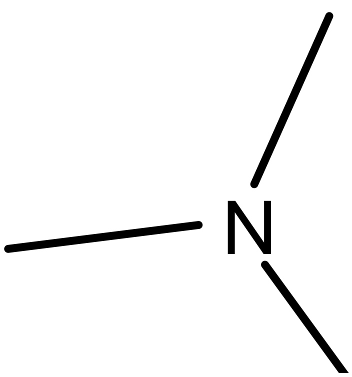
Yield; 93%, red solid, m. p = 110-112 ºC.

HRMS (ESI): calcd. for $C_{33}H_{28}N_3O_2$ [M+H]$^+$: 498.21815, found: 498.21760 .

^{1}H NMR (DMSO): 13.11 (s, NH), 9.61 (d, *J* = 8.4Hz, 1H, H-5), 8.54 (s, 1H, H-3), 8.29 (d, *J* = 8.0 Hz, 2H, H-2`/H-6`),), 8.07 (d, *J* = 8.3 Hz,1H, H-8) 7.78 (t, *J* = 7.2 Hz, 1H, H-7), 7.64(t, *J* = 7.1 Hz, 1H, H-6), 7.51(m, 4H), 7.37(d, *J* = 7.9 Hz, 2H), 6.93-7.16 (m, 4H), 3.68 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3) .

^{13}C NMR (DMSO-d_6): 156.0, 149.3, 143.5, 139.9, 136.3, 135.2, 130.6, 130.3, 130.0, 129.9, 128.7, 127.8, 127.7, 127.2, 124.0, 116.5, 114.8, 114.3, 55.6, 21.5.

4,4`-(2-(2-*p*-Tolylquinolin-4-yl)-1*H*-imidazole-4,5-diyl)bis(N,N-dimethylaniline) (71f)



Yield; 93%, brownish solid, m. p = 140-142 ºC.

HRMS (ESI): calcd. for $C_{35}H_{34}N_5$ $[M+H]^+$: 524.28142, found:524.28087.

^{1}H NMR (DMSO-d$_6$): δ 12.94 (brs, 1H, NH), 9.70 (d, *J* = 8.4 Hz, 1H, H-5), 8.54 (s, 1H, H-3), 8.30 (d, *J* = 7.9 Hz, 2H, H-2\`/H-6\`), 8.06 (d, *J* = 8.3 Hz, 1H, H-8), 7.76 (t, *J* = 7.6 Hz, 1H, H-7), 7.63 (d, *J* = 7.3 Hz, 1H, H-6), 7.43-7.46 (m, 4H), 7.36 (d, *J* = 7.9 Hz, 4H), 6.73 (d, *J* = 7.4 Hz, 2H), 2.89 (brs, 12H, phenyl-N(CH_3)$_2$), 2.37 (s, 3H, phenyl-CH_3).

4-(4, 5-Di(pyridin-2-yl)-1*H*-imidazol-2-yl)-2-*p*-tolylquinoline (71g)

Yield; 93%, yellow solid, m.p = 80-82 ºC.

HRMS (ESI): calcd. for $C_{29}H_{22}N_5$ $[M+H]^+$: 440.18752, found: 440.18714.

^{1}H NMR (DMSO-d$_6$): δ 9.33 (d, *J* = 8.3Hz, 1H, H-5), 9.08 (s, 1H), 8.84 (brs, 1H), 8.68 (s, 1H, H-3), 8.32 – 8.40 (m, 3H), 8.10 – 8.13 (m, 2H), 7.75-7.79 (m, 2H), 7.67 (t, *J* = 7.1 Hz, 1H, H-6), 7.56 (brs, 1H), 7.39 (d, *J* = 7.8 Hz, 2H), 6.98-7.09 (m, 1H), 6.63 (d, *J* = 8.3 Hz, 1H) .

^{13}C NMR (DMSO-d$_6$): δ 156.1, 149.1, 140.1, 137.3, 136.1, 130.5, 130.1, 129.9, 127.8, 127.6, 127.2, 124.0, 118.5, 115.1, 115.1, 21.5.

4-(4,5-Di(thiophen-2-yl)-1*H*-imidazol-2-yl)-2-*p*-tolylquinoline (71h)

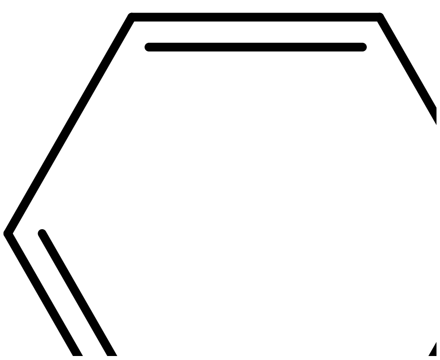
Yield; 95%, orange solid, m. p = 245-248ºC.

HRMS (ESI): calcd. for $C_{27}H_{20}N_3S_2$ $[M+H]^+$: 450.10986, found: 450.10932 .

^{1}H NMR (DMSO-d$_6$): 9.48 (d, *J* = 7.7 Hz, 1H, H-5), 8.53 (s, 1H, H-3), 8.27 (d, *J* = 9.0 Hz, 2H, H-2`/ H-6`), 8.09 (d, *J* = 9.0 Hz, 1H, H-8), 7.80 (dt, *J* = 6.9 Hz, *J* = 1.3 Hz, 1H, H-7), 7.63- 7.69 (m, 1H, H-6), 7.07- 7.50 (m, 8H), 2.38 (s, 3H, C*H*3).

^{13}C NMR (DMSO-d$_6$): 156.1, 149.2, 144.4, 140.0, 136.2, 134.7, 130.8, 130.4, 130.1, 129.9, 129.6, 128.7, 128.1, 127.7, 127.4, 124.5, 123.9, 117.0, 21.4.

2-(2-*p*-Tolylquinolin-4-yl)-1*H*-phenanthro[9,10-d]imidazole (71i)



Yield; 92%, brown solid, m. p = 195-197 ºC.

HRMS (ESI): calcd. for $C_{31}H_{22}N_3$ $[M+H]^+$: 436.18137, found: 436.18082

^{1}H NMR (DMSO-d$_6$): δ 13.90 (s, 1H, NH), 9.58 (d, *J* = 7.8 Hz, 1H, H-5), 8.84-8.90 (m, 2H),8.70 (s, 1H, H-3), 8.69 (d, *J* = 6.3 Hz,1H), 8.59 (d, *J* = 7.8 Hz,1H), 8.33 (d, *J* = 8.2 Hz, , H-2`/ H-6`),), 8.15 (d, *J* = 7.9 Hz, 1H, H-8), 7.85-7.65 (m, 6H), 7.41 (d, *J* = 8.1 Hz, 2H, H-3`/ H-5`), 2.56 (s, 3H, C*H*$_3$).

^{13}C NMR (DMSO-d$_6$): δ 156.2, 149.3, 147.5, 140.1, 138.1, 136.2, 135.9, 130.5, 130.2, 130.0, 128.8, 128.3, 128.0, 127.7, 127.5, 127.4, 126.5, 126.1, 124.8, 124.3, 122.9, 122.7, 122.6, 118.2, 21.5 .

2-(2-*p*-Tolylquinolin-4-yl)-1*H*-imidazo[4,5-*f*][1,10]phenanthroline (71j)

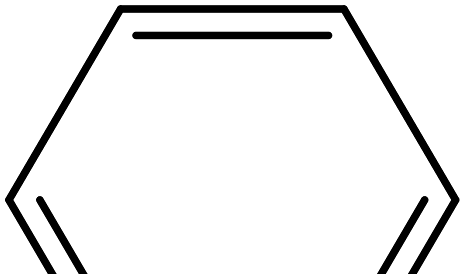
Yield; 93%, yellow solid, m. p = 250-251 ºC.

HRMS (ESI): calcd. for $C_{29}H_{20}N_5$ [M+H]$^+$: 438.17187, found: 438.17132

^{1}H NMR (DMSO-d$_6$): δ 9.45 (d, *J* = 8.4 Hz, 1H, H-5), 9.02 (d, *J* = 2.7 Hz, 2H), 8.92 (d, *J* = 8.0 Hz, 2H,), 8.61 (s, 1H, H-3), 8.26 (d, *J* = 8.0 Hz, 2H , H-2`/H6`), 8.12 (d, *J* = 8.4 Hz, 1H, H-8), 7.78-7.80 (m, 3H), 7.70 (dd, *J* = 7.0 Hz, *J* = 7.0 Hz, 1H, H-6), 7.37 (d, *J* = 8.0, 2H, H-3`/H-5`), 2.38 (s, 3H, C*H*$_3$).

^{13}C NMR (DMSO-d$_6$): δ 156.2, 149.2, 148.8, 144.4, 140.2, 136.0, 135.9, 130.7, 130.5, 130.2, 130.1, 127.7, 127.3, 124.2, 124.0, 118.5, 21.5.

4-(4,5-Biphenyl-1*H*-imidazol-2-yl-)-2-(4-fluorophenyl)quinoline (72a)



HRMS (ESI): calcd. for $C_{30}H_{19}FN_3$ $[M\text{-}H]^-$: 440.15630, found: 440.15685

Yield; 98%, yellow solid, m.p = 280-281 ºC.

^{1}H NMR (DMSO-d$_6$): δ 13.26 (s, 1H, NH), 9.62 (d, *J* = 7.8 Hz, 1H, H-5), 8.58 (s, 1H, H-3), 8.43 (dd, *J* = 8.8 Hz, *J* = 5.6 Hz, 2H, H-2`/H-6`), 8.11 (d, *J* = 7.9 Hz, 1H, H-8), 7.81 (dt, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H, H-7), 7.68 (t, *J* = 7.9 Hz, 1H, H-6), 7.57-7.64 (m, 4H), 7.25-7.51(m, 8H).

^{13}C NMR (DMSO-d$_6$): δ 165.5, 162.2, 155.1, 149.2, 144.1, 138.7, 135.6, 135.5, 135.3, 135.2, 131.2, 130.4, 130.1, 130.0, 129.9, 129.3, 129.3, 128.9, 128.8, 127.7, 127.6, 127.5, 127.4, 124.0 116.8, 116.4, 116.1 .

4-(4,5-Bis(4-bromophenyl)-1*H*-imidazol-2-yl-)-2-(4-fluorophenyl)quinoline (72b)

Yield;97%, yellow solid, m.p = 270-272 ºC.

HRMS (ESI): calcd. for $C_{30}H_{19}Br_2FN_3$ $[M+H]^+$: 597.99298, found: 597.99243 .

^{1}H NMR (DMSO-d$_6$): δ 13.34 (s, 1H, NH), 9.50 (d, *J* = 7.6 Hz, 1H, H-5), 8.53 (s, 1H, H-3), 8.39 (d, *J* = 6.3, 2H, H-2\`/ H-6\`), 8.09 (d, *J* = 7.8 Hz, 1H, H-8), 7.40-7.82 (m, 12H).

4-(4,5-Bis(4-fluorophenyl)-1*H*-imidazol-2-yl-)-2-(4-fluorophenyl)quinoline (72c)

Yield; 93%, white solid, m.p = 315-318 ºC.

HRMS (ESI): calcd. for $C_{30}H_{19}F_3N_3$ $[M+H]^+$: 478.15311, found: 478.15256 .

^{1}H NMR (DMSO-d$_6$): δ 13.28 (s, 1H, NH), 9.57 (d, *J* = 8.5, 1H, H-5), 8.55 (s, 1H, H-3), 8.42 (dd, *J* = 8.3 Hz, *J* = 5.7 Hz, 2H, H-2\`/ H-6\`), 8.09 (d, *J* = 8.3 Hz, 1H, H-8),7.79 (t, *J* = 8.1 Hz, 1H, H-7), 7.67 (t, *J* = 7.6 Hz, 1H, H-6), 7.59-7.64 (m, 4H), 7.40(dd, *J* = 8.8 Hz, *J* = 8.8 Hz, 2H, H-3\`/ H-5\`), 7.21-7.66 (m, 4H).

^{13}C NMR (DMSO-d$_6$): δ 165.5, 162.2, 155.1, 149.2, 144.1, 135.5, 135.5, 135.2, 131.5, 130.5, 130.0, 129.9, 129.5, 127.6, 127.6, 123.9, 116.9, 116.4, 116.1, 115.9 .

4-(4,5-Di-*p*-toly-l*H*-imidazol-2-yl-)-2-(4-fluorophenyl)quinoline (72d)

Yield; 97%, white solid, m.p = 274ºC.

HRMS (ESI): calcd. for $C_{32}H_{25}FN_3$ $[M+H]^+$: 470.20325, found:470.20270.

^{1}H NMR (DMSO-d$_6$): δ 13.16 (s, 1H, NH), 9.60 (d, *J* = 8.5 Hz, 1H , H-5), 8.56 (s, 1H, H-3), 8.42 (dd, *J* = 8.8 Hz, *J* = 5.6 Hz, 2H, H-2\`/ H-6\`), 8.09 (d, *J* = 8.3 Hz, 1H, H-8), 7.79 (dt, *J* = 6.9 Hz, *J* = 1.3Hz, 1H, H-7),7.67 (dt, *J* = 7.2 Hz, *J* = 1.1 Hz, 1H, H-6), 7.38 – 7.44 (m, 4H),7.41 (t, *J* = 8.8 Hz, 2H, H-3\`/ H5\`),7.28 (d, *J* = 7.4 Hz, 2H), 7.15 (d, *J* = 7.5 Hz, 2H), 2.34 (s, 3H, -CH_3), 2.28 (s, 3H , CH_3).

^{13}C NMR (DMSO-d$_6$): δ 165.5, 162.2, 155.1, 149.2, 143.8, 138.1, 136.5, 135.6, 135.4, 132.5, 130.4, 130.1, 130.0. 129.9, 129.5, 129.0, 128.3, 127.8, 127.6, 127.5, 124.0, 116.7, 116.4, 116.1, 21.4.

4-(4,5-Bis(4-methoxyphenyl)-1*H*-imidazol-2-yl-)-2-(4-fluorophenyl)quinoline (72e)



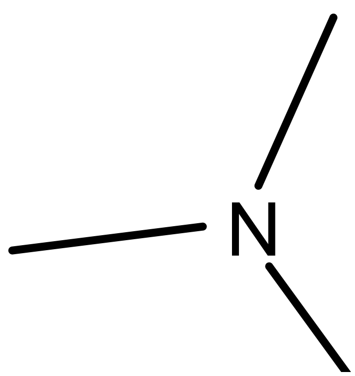
Yield; 95%, red solid, m.p = 98 ºC.

HRMS (ESI): calcd. for $C_{32}H_{25}FN_3O_2$ $[M+H]^+$: 502.19308, found:502.19253.

^{1}H NMR (DMSO-d$_6$): δ 13.01 (s, 1H, NH), 9.63 (dd, *J* = 8.5 Hz, *J* = 0.9 Hz, 1H, H-5), 8.54 (s, 1H, H-3), 8.42 (dd, *J* = 8.9 Hz, *J* = 5.6 Hz, 2H, H-2`/ H-6`), 8.08 (dd, *J* = 8.4 Hz, *J* = 0.7 Hz, 1H, H-8), 7.76-7.84 (m, 1H, H-7), 7.63-7.68 (m, 1H, H-6), 7.56 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 8.8 Hz, 2H), 7.39 (t, *J* = 8.9 Hz, 2H, H-3`/ H-5`), 7.04 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H, CH_3), 3.75 (s, 3H, CH_3).

^{13}C NMR (DMSO-d$_6$): δ 165.5, 165.3, 162.2, 159.8, 158.8, 155.2, 149.3, 143.4, 138.3, 135.7, 135.7, 135.5, 132.5, 130.6, 130.3, 130.0, 129.9, 128.9, 128.8, 128.0, 127.8, 127.3, 124.0, 123.6, 116.5, 116.3, 116.0, 115.3, 114.8, 114.4 , 55.8, 55.6

4,4`-(2-(2-(4-Fluorophenyl)quinolin-4-yl)-1*H*-imidazole-4,5-diyl)bis(N,N-dimethylaniline) (72f)

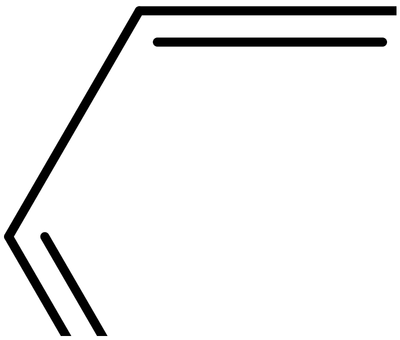


Yield; 96%, brownish solid, m.p = 140-142 ºC.

HRMS (ESI): calcd. for $C_{34}H_{31}FN_5$ $[M+H]^+$: 528.25635, found:528.25580.

^{1}H NMR (DMSO-d$_6$): δ 13.00 (brs, 1H, NH), 9.70 (d, *J* = 8.3 Hz, 1H, H-5), 8.55 (s, 1H, H-3), 8.41-8.45 (m, 2H, H-2`/H-6`), 8.07 (d, *J* = 8.3 Hz, 1H, H-8), 7.78 (dd, *J* = 7.7 Hz, *J* = 7.7Hz, 1H, H-7), 7.65 (t, *J* = 7.3 Hz, 1H, H-6), 7.37-7.43 (m, 6H), 6.74 (d, *J* = 7.4 Hz, 4H), 2.90 (brs, 12H, phenyl-N-(CH_3)$_2$).

4-(4,5-Di(pyridine-3-yl)-1*H* –imidazol-2-yl)-2-(4-fluorophenyl)quinoline (72g)



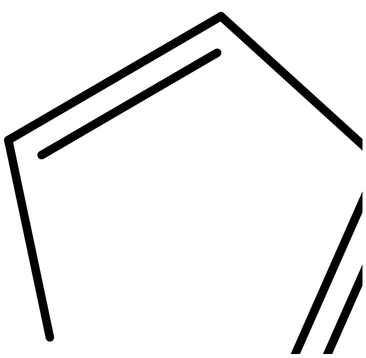
Yield; 93%, yellow solid, m.p = 134-135 ºC.

HRMS (ESI): calcd. for $C_{28}H_{19}FN_5[M+H]^+$: 444.16245, found:444.16190.

^{1}H NMR (DMSO-d$_6$): δ 14.18 (s, 1H, NH), 9.62 (d, *J* = 8.3 Hz, 1H, H-5), 9.43 (d, *J* = 8.4 Hz, 2H), 7.14-8.73 (m, 14H).

^{13}C NMR (DMSO-d$_6$): δ 165.5, 162.3, 155.1, 149.1, 148.3, 135.5, 135.1, 134.9, 130.7, 130.5, 130.2, 130.1, 127.7, 127.4, 124.0, 123.9, 123.6, 118.2, 116.5, 116.4, 116.2, 116.1.

4-(4,5-Di(thiophen-2-yl)-1*H*-imidazol-2-yl-)-2-(4-fluorophenyl)quinoline (72h)



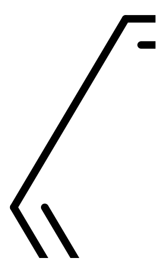
Yield; 99%, brown solid, m.p = 306-308 ºC.

HRMS (ESI): calcd. for $C_{26}H_{17}FN_3S_2[M+H]^+$: 454.08479, found:454.08424.

^{1}H NMR (DMSO-d$_6$): δ 13.43 (s, 1H, NH), 9.49 (d, *J* = 7.8 Hz, 1H, H-5), 8.54 (s, 1H, H-3), 8.42 (t, *J* = 8.9 Hz, 2H, H-2\`/ H-6\`), 8.10 (d, *J* = 7.8 Hz, 1H, H-8), 7.81 (dt, *J* = 8.2 Hz, *J* = 1.3 Hz, 1H, H-7), 7.77 (d, *J* = 5.9 Hz, 1H), 7.68 (dt, *J* = 8.2 Hz, *J* = 1.2 Hz, 1H, H-6), 7.50 (brs, 1H), 7.46 (d, *J* = 4.8 Hz, 1H), 7.41 (t, *J* = 8.9 Hz, 2H, H-3\`/ H-5\`), 7.25 (brs, 2H), 7.04 (brs, 1H).

^{13}C NMR (DMSO-d$_6$): δ 165.5, 162.2, 155.1, 149.2, 144.3, 135.4, 134.8, 130.5, 130.0, 130.1, 130.0, 129.7, 128.7, 128.3, 128.1, 127.6, 127.4, 125.8, 124.4, 123.9, 117.0, 116.4, 116.1 .

2-(2-(4-Fluorophenyl)quinolin-4-yl)-1*H*-phenanthro[9,10-*d*]imidazole (72i)



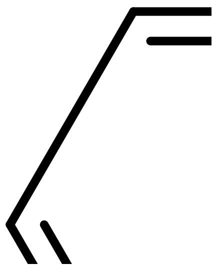
Yield; 97%, brown solid, m.p = 183-185 ºC.

HRMS (ESI): calcd. for $C_{30}H_{19}FN_3$ $[M+H]^+$: 440.15630, found: 440.15575 .

^{1}H NMR (DMSO-d$_6$): δ 13.91 (s, 1H, NH), 9.59 (d, *J* = 8.4 Hz, 1H, H-5), 8.87 (dd, *J* = 12.1 Hz, *J* = 8.4 Hz, 2H), 8.70 (s, 1H, H-3), 8.68 (d, *J* = 8.1 Hz, 1H), 8.56 (d, *J* = 7.8 Hz, 1H), 8.47 (dd, *J* = 8.7 Hz, *J* = 5.6 Hz, 2H, H-2\`/H-6\`), 8.16 (d, *J* = 8.3 Hz, 1H, H-8), 7.85 (dt, *J* = 7.1Hz, *J* = 1.0 Hz, 1H, H-7), 7.62 – 7.79 (m, 5H), 7.45 (t, *J* = 8.8 Hz, 2 H).

^{13}C NMR (DMSO-d$_6$): δ 165.5, 162.3, 155.2, 149.2, 147.4, 138.1, 136.0, 130.7, 130.2, 130.1, 128.3, 128.3, 128.0, 127.9, 127.7, 127.6, 126.6, 126.1, 124.8, 124.4, 124.3, 122.9, 122.6, 118.3, 116.5, 116.2 .

2-(2-(4-Fluorophenyl)quinolin-4-yl)-1*H*- imidazo[4,5-*f*][1,10]phenanthroline (72j)



Yield; 94%, yellow solid, m.p = 320-322 ºC.

HRMS (ESI): calcd. for $C_{28}H_{17}FN_5$ $[M+H]^+$: 442.14680, found: 442.14625 .

^{1}H NMR (DMSO-d$_6$): δ 9.55 (d, *J* = 8.4 Hz, 1H, H-5), 9.04 (d, *J* = 5.43 Hz, 2H), 8.78 (s, 1H, H-3), 8.48 (dd, *J* = 8.7 Hz, *J* = 5.7 Hz, 2H, H-2`/H-6`), 8.13 (d, *J* = 8.2 Hz, 1H, H-8), 7.65-7.89 (m, 6H), 7.41 (dd, *J* = 8.8 Hz, *J* = 8.8 Hz, 2 H).

^{13}C NMR (DMSO-d$_6$): δ 169.6, 162.2, 155.2, 149.2, 148.7, 148.4, 144.3, 135.9, 135.4, 130.9, 130.7, 130.2, 130.1, 127.9, 127.5, 124.3, 124.2, 124.0, 123.5, 118.6, 116.4, 116.2.

4. Results and discussion

4.1. Preperation of 2-aryl-quiniline-4-carboxylic acids (64a-d)

Scheme 17. Synthesis of 2-aryl-quiniline-4-carboxylic acids (**64a-d**).

The synthesis of the title compounds was achieved *via* Pfitzinger methodology. In which an appropriate substituted acetophenone was reacted with isatin in refluxing ethanol at 80 °C For 24h in presence of NaOH as in Scheme 17. The desired acid was collected after acidification with cold hydrochloric acid. The acids were recrystallized to give pure compounds in yields ranging from 90% to 95%. This conventional method can be used up to 30 g starting material. Although, microwave organic synthesis was used to produce compound **64a** (El Ashry *et al.*, 2005). Microwave technique was used to synthesis of **64a-d** in which all of these compounds were obtained in an excellent yields and a very short time.

The structures of compounds **64a-d** were supported by spectral (NMR and MS) data. Previously these acids were prepared by different groups (Buu *et al*., 1949) (Obushak *et a*l., 2006) (Wang *et al*., 2009) (DuPuis and Lindwall, 1934).

The various ^{1}H and ^{13}C-NMR signals were assigned based on DEPT and 2D NMR (HMQC) experiments which showed the correct signals. The ^{1}H-NMR spectra showed the carboxylic acids proton around 14 ppm as a broad singlet, while the H-5 proton appeared as a doublet signal at about 8.61 ppm (*J* = 8 Hz). The H-3 proton of this series resonates as a sharp singlet around δ 8.4 ppm. The H-8 proton resonates as a doublet in the range 8.07-8.14 ppm with (*J* = 8 Hz). The H-7 proton resonates as a multiplet in the range 7.76-7.85 ppm, while H-6 proton resonates as a multiplet in the range 7.61-7.70 ppm.

The ^{13}C-NMR spectra indicate the presence of the carbonyl carbon of the carboxylic acid group resonating at 168.0-168.2 ppm. The C-2 carbon resonates in the range 155.0-156.3 ppm, while the rest of aromatic carbons resonate around 119, 138, 124, 126, 128, 131, 130 and 149 ppm, assigned to C-3, C-4, C-4a , C-5, C-6 , C-7 , C-8, and C-8a`, respectively.

2-Phenylquinoline-4-carboxylic acid (64a).

Previously synthesized by Dupuis (Dupuis and lindwell, 1934), the compound was characterized through the different spectroscopic methods. In the ^{1}H-NMR spectrum, the phenyl group protons resonate at 7.58 -7.78 and 8.27 ppm for H-4`/H-3`/H-5` and H-2`/H-6`, respectively. The other protons resonate in the ranges indicated above for this series. In the $^{13}C$-NMR spectrum, the carbons of the phenyl group resonate at 129.5, 130.5, 127.7 and 138.4 ppm, assigned to C-3`/C-5`, C-4`, C-2`/C-6` and C-1`, respectively.

2-(4-Chlorophenyl)quinoline-4-carboxylic acid (64b).

Previously synthesized by wang (wang *et al*., 2009), this known compound was characterized through the different spectroscopic methods**.** In the ^{1}H-NMR spectrum, the

phenyl protons appears as two doublets, which is typical of 1,4-disubstituted benzene rings at δ 7.52 and 8.22 ppm for H-3`/H-5` and H-2`/H-6`, respectively.. In the ^{13}C-NMR spectrum, the carbons of the C(2)-phenyl group resonate at 129.4, 135.4, 128.4 and 138.1 ppm, assigned to C-3`/C-5`, C-4`, C-2`/C-6` and C-1`, respectively.

2-*p*-Tolylquinoline-4-carboxylic acid (64c).

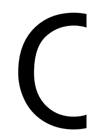
Previously synthesized by Obushak (Obushak *et a*l., 2006), this known compound was characterized through the different spectroscopic methods**,** The ^{1}H-NMR spectrum of the compound shows the phenyl ring protons as two doublets at 7.34 and 8.22 ppm for H-3`/H-5` and H-2`/H-6`, respectively. The (C4`)-methyl group protons appears as a sharp singlet signal at 2.35 ppm,. In the $^{13}$C-NMR spectrum, the carbons of the C(2)-phenyl group resonate at 130.2, 135.6, 127.6 and 140.3 ppm, assigned to C-3`/C-5`, C-4`, C-2`/C-6` and C-1`, respectively, while (C4`)-methyl group carbon appears at 21.4 ppm.

2-(4-Fluorophenyl)quinoline-4-carboxylic acid (64d).

Previously synthesized by Buu (Buu *et al*., 1949), the title compound was characterized by its spectral data**,** The ^{1}H-NMR spectrum, exhibits the C(2)-phenyl group proton H-3`/H-5` and H-2`/H-6`resolved doublet of doublet at 7.34 with ($^{3}J_{H\text{-}F}$ = 8.9 Hz) and 8.27 ppm with ($^{4}J_{H\text{-}F}$ = 5.6 Hz) respectively, due to spin-spin coupling interaction with the fluorine atom.

In the ^{13}C-NMR spectrum of compound **64d** reveal clearly the presence of the fluorine atom and its effect on the adjacent carbons. The phenyl group carbons resonate at 116.3 (d, $^{2}J_{C\text{-}F}$ = 21.5 Hz), 130.0 (d, $^{3}J_{C\text{-}F}$ = 8.6 Hz), 134.8 (d, $^{4}J_{C\text{-}F}$ = 2.9 Hz), and 163.9 (d, $^{1}J_{C\text{-}F}$ = 246.2 Hz) ppm, assigned to C-3`/C-5`, C-2`/C-6`, C-1` and C-4`, respectively.

4.2. Preparation of Ethyl 2-aryl-quinoline -4-carboxylate (65a-d)



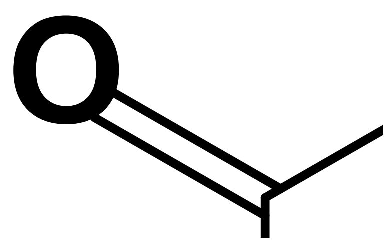
Scheme 18. Synthesis of ethyl 2-aryl- quinoline -4-carboxylate (**65a-d**)

Esterification of the acids was preformed using both the conventional and microwave methods to produce the known compounds **65a-d** (El Ashry *et al.*, 2005) (Leardin *et al*., 1984) (John *et al*., 1931) (Duvelleroy., 2005)**.** In both methods the acids were dissolved in ethanol with catalytic amount of H_2SO_4 as in Scheme 18 (Rasras *et al.,* 2010). Upon completion of the reaction the esters were isolated.

The structures of **65a-d** were in full agreement with their spectral (^{1}H-NMR and MS) data. ^{1}H-NMR shows the disappearance of the broad signal at about 14 (CO_2H proton) present in the spectra of the corresponding acid and the appearance instead of the ethyl protons peaks: CH_2 as a quartet signal in the range 4.45-4.53 ppm and CH_3 as a triplet signal in the range 1.39-1.48 ppm. The rest of the protons on the quinoline scaffold resonate approximately at the same δ values of the corresponding acids. ^{13}C-NMR spectra show the appearance of ethyl carbons peaks at about 62.0 and 14.5 for CH_2 and CH_3 carbons respectively. In the ^{13}C-NMR spectrum, the carbon of the carboxylate group [*C*OOEt] for

65a-d resonates in the range (166.2-166.4 ppm), which is more shielded than the corresponding in compounds **64a-d** (168.1-168.4 ppm).

4.3. Preparation of 2-aryl- quinoline -4-yl)methanols (66a-d)



Scheme 19. Synthesis of 2-aryl- quinoline -4-yl)methanols **(66a-d)**

Reduction of the esters **65a-b** to alcohols **66a-d** was performed using sodium borohydride in refluxing aqueous ethanol as in Scheme 19. The alcohols were isolated with good yields (72-88%), only **66a** was synthesized previously by DasGupta (DasGupta *et al.*, 2009). It is worth mentioning that Lithium aluminum hydride did not work well in this type of reduction.

The structures of **66a-d** are supported by their ^{1}H-NMR ,^{13}C-NMR and MS spectral data. ^{1}H-NMR shows the disappearance of ethyl protons peaks present in the spectra of the starting esters and the appearance instead of a singlet signal integrating for two protons in the range 5.06-5.16 ppm for CH_2O group protons. Another signal integrating for one proton and resonating at variable position was assigned to the exchangeable proton of the hydroxyl group (O*H*). The rest of the aromatic protons resonate at the same δ values as these of the corresponding ester compounds. ^{13}C-NMR spectra show the disappearance of ethyl carbons

peaks and the carbonyl ester peaks (in the spectra of the starting compounds **65a-d** from the spectra and appearance of the (CH_2) carbon signal at around 62 ppm.

4.4. Preparation of 2-aryl-quinoline-4-carboxaldehyde (67a-d)



Scheme 20. Synthesis of 2-aryl-quinoline-4-carboxaldehyde

Pyridinium chlorochromate (PCC) was used to oxidize the alcohol to get the desired aldehyde. Low yield and difficult purification of the resulting aldehyde made it difficult to produce this compound in a good quantity. Oxidation of the alcohol compounds to the corresponding aldehyd in a good yield (60-70) was successfully achieved using selenium oxide as an oxidizing agent. It is worth mentioning that compound **67a** and **67b** were previously prepared in the literature by Tarbell (Tarbell *et al.*, 1945) and Molina (Molina *et al.*, 1993), respectivily.

The structures of compounds **67a-d** are supported by their ^{1}H-NMR, ^{13}C-NMR and MS spectral data. ^{1}H-NMR of each compound shows the disappearance of the methylene and alcohol protons (CH_2OH) peaks present in starting compounds and the appearance of a one proton singlet at about 10.5 ppm assigned for the aldehyde (C*H*O) proton. Also, the ^{13}C-

NMR spectra show the disappearance of the methylene (CH_2OH) carbon signal from the spectrum and appearance of the (CHO) carbon signal in the range 192.8-195.4 ppm.

The ^{1}H-NMR spectrum for the compounds **64-67d** the C(2)-phenyl H-3`/H-5` and H-2`/H-6`protons group of (**64-67d**) series is well characterized as a sharp doublet of doublet in the ranges 7.20-7.39 with ($^{3}J_{H\text{-}F}$ = 8.7-8.9 Hz) and 8.15-8.36 ppm with ($^{4}J_{H\text{-}F}$ = 5.5-5.6 Hz) respectively due to spin-spin coupling interaction with the vicinal fluorine atom, the other protons resonate in the ranges indicated above for this series.

In the ^{13}C-NMR spectrum, The spectra of compounds **64-67d** reveal clearly the presence of the fluorine atom and its effect on the adjacent carbons, The carbons of the C(2)-phenyl group resonate as doublet signals at about 116 (d, $^{2}J_{C\text{-}F}$ = 23.3 Hz), 130 (d, $^{3}J_{C\text{-}F}$ = 8.3 Hz), 135 and 164 (d, $^{1}J_{C\text{-}F}$ = 245.8 Hz) ppm, assigned respectively to C-3`/C-5`, C-2`/C-6`, C-1` and C-4`. The other carbons resonate in the ranges indicated above for this series.

4.5. Preparation of imidazolyl quinoline (69a-j, 70a-j, 71a-j and 72a-j)

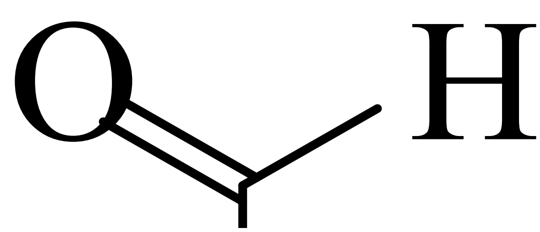
The conventional method based on Radiszewski method for imidazol synthesis was used for the preparation of the desired compounds. This conventional method is worked very nicely, but longe time of reaction was needed. Shorter time of reaction was achieved using the microwave technology. Scheme 21 shows the microwave synthesis of the 4-imidazoly-2-phenylquinoline compounds, in which quinolionecarboxaldehyde **67a** was reacted with various symmetrical diketones (**68a-f**) under microwave irradiation.



Scheme 21. Synthesis of compounds **69a-f**

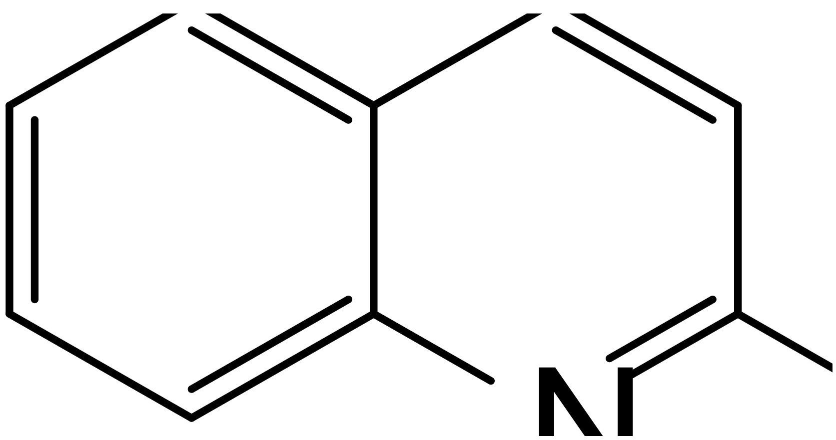
The reaction proceeded very nicely. TLC showed the completion of the reaction in 12 minuets. Work up and crystallization of the product afforded a pure sample which was analyzed and proved to be in agreement with the expected structure.

On the top of the previous diketones, a hetero aromatic diketone **68g** and **68h** were used to prepare the new imidazolylquinolines **69h** and **69g** as shown in Scheme 22. The reaction proceeds as for compounds **69a-f.**



Scheme 22. Synthesis of compounds **69h** and **69g**

Also tricyclic diketones **68i** and **68j** were used to prepare the new compounds **69i** and **69j** as shown in Scheme 23.



Scheme 23. Synthesis of compounds **69i** and **69j**

All of the new compounds gave satisfactory physicochemical analyses. In these analyses we used mainly HRMS, ^{1}H-NMR and ^{13}C-NMR Figures 38 to 100. All ^{1}H-NMR spectra of the new compounds show appearance of broad singlet signal in the range 12.93-14.18 assigned to NH, which is typical for the NH of the imidazole ring as an example Figure 42. As it is seen, all the new compounds are aromatic compounds, the ^{1}H-NMR spectra show

overlapping signals for most of the benzene ring protons except for those with specific signals like **69d** in which two signals integrating for 3 protons are assigned for the methyl groups resonating at 2.29 and 2.35 ppm Figure 3. While ^{13}C-NMR spectrum shows two peaks resonating at 21.4 and 21.3 assigned for two *para* substituted methyl groups Figure 4. Compound 69e also shows two signals integrating for 3 protons assigned for the methoxy groups resonating at 3.79 and 3.74 ppm Figure 5, while ^{13}C-NMR spectrum shows two peaks resonating at 55.8 and 55.6 assigned for two *para* substituted methoxy group Figure 6. Otherwise, in compound **69f** the ^{1}H-NMR spectrum shows broad singlet signal integrating for 12 protons which are assigned for the N-methyl groups resonating at 2.96 ppm.

Microwave synthesis was used to react the quinoline carbaldehyde **67b**, **67c** and **67d** with the diketones **68a-j** as in Scheme 18, 19 and 20 to produce 30 new compounds **70a-j**, **71a-j** and **72a-j**. All of these new compounds, Table 1and 2, were purified (as illustrated in the experimental part) and identified using spectroscopic techniques. The structures and the spectroscopic data for these new compounds were in full agreements with each other

Table1

compound	X	R_1	compound	X	R_1
69a	H	phenyl	71a	CH_3	phenyl
69b	H	4-bromophenyl	71b	CH_3	4-bromophenyl
69c	H	4-Fluorophenyl	71c	CH_3	4-Fluorophenyl
69d	H	4-methylphenyl	71d	CH_3	4-methylphenyl
69e	H	4-methoxyphenyl	71e	CH_3	4-methoxyphenyl
69f	H	4-dimethylaminophenyl	71f	CH_3	4-dimethylaminophenyl
69g	H	2-pyridyl	71g	CH_3	2-pyridyl
69h	H	2-thiyl	71h	CH_3	2-thiyl
70a	Cl	phenyl	72a	F	phenyl
70b	Cl	4-bromophenyl	72b	F	4-bromophenyl
70c	Cl	4-Fluorophenyl	72c	F	4-Fluorophenyl
70d	Cl	4-methylphenyl	72d	F	4-methylphenyl
70e	Cl	4-methoxyphenyl	72e	F	4-methoxyphenyl
70f	Cl	4-dimethylaminophenyl	72f	F	4-dimethylaminophenyl
70g	Cl	2-pyridyl	72g	F	2-pyridyl
70h	Cl	2-thiyl	72h	F	2-thiyl

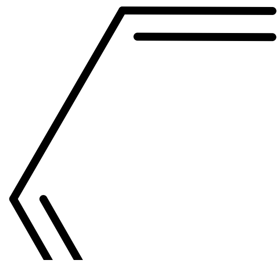


Table 2

compound	69i	69j	70i	70j	71i	71j	72i	72j
R	H	H	Cl	Cl	CH_3	CH_3	F	F
X	CH	N	CH	N	CH	N	CH	N

These new compounds represents new library of compounds with a bioactive chromophor in their scaffold. Potential bioactivities for this library of compounds might be in the field of antibiotics and cancer. Further screening for this library will reveal the importance of this library.

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6. Appendix

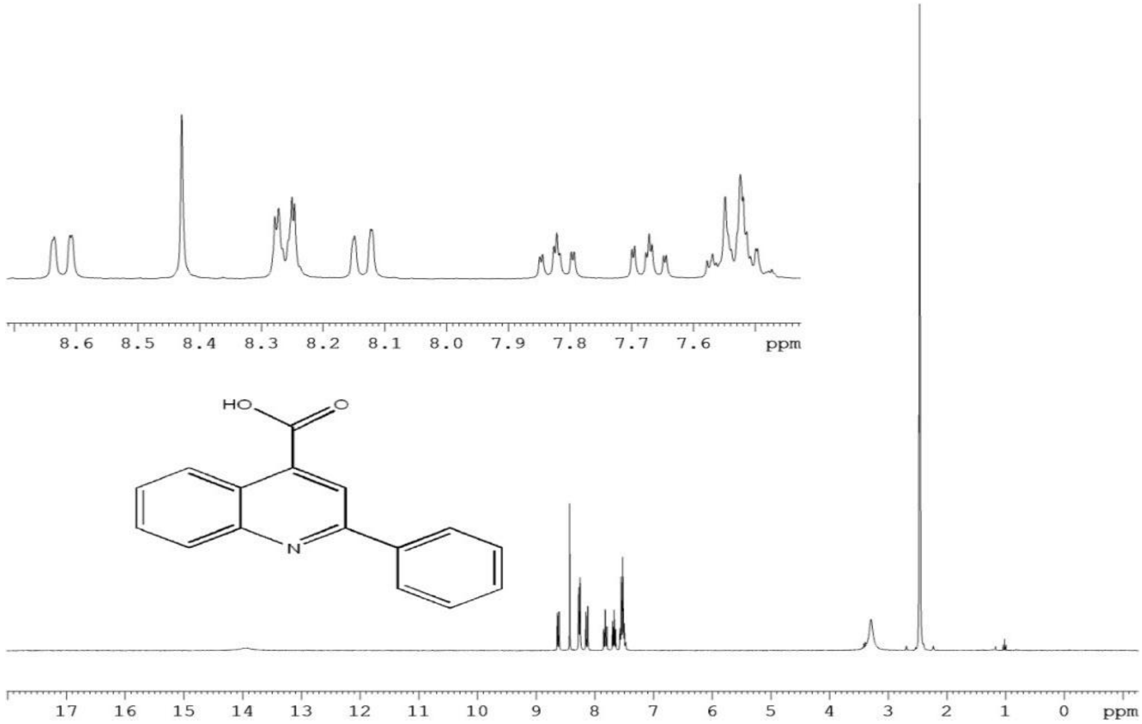


Figure 3. ^{1}H-NMR spectrum of compound [**64a**] (DMSO-d_6).

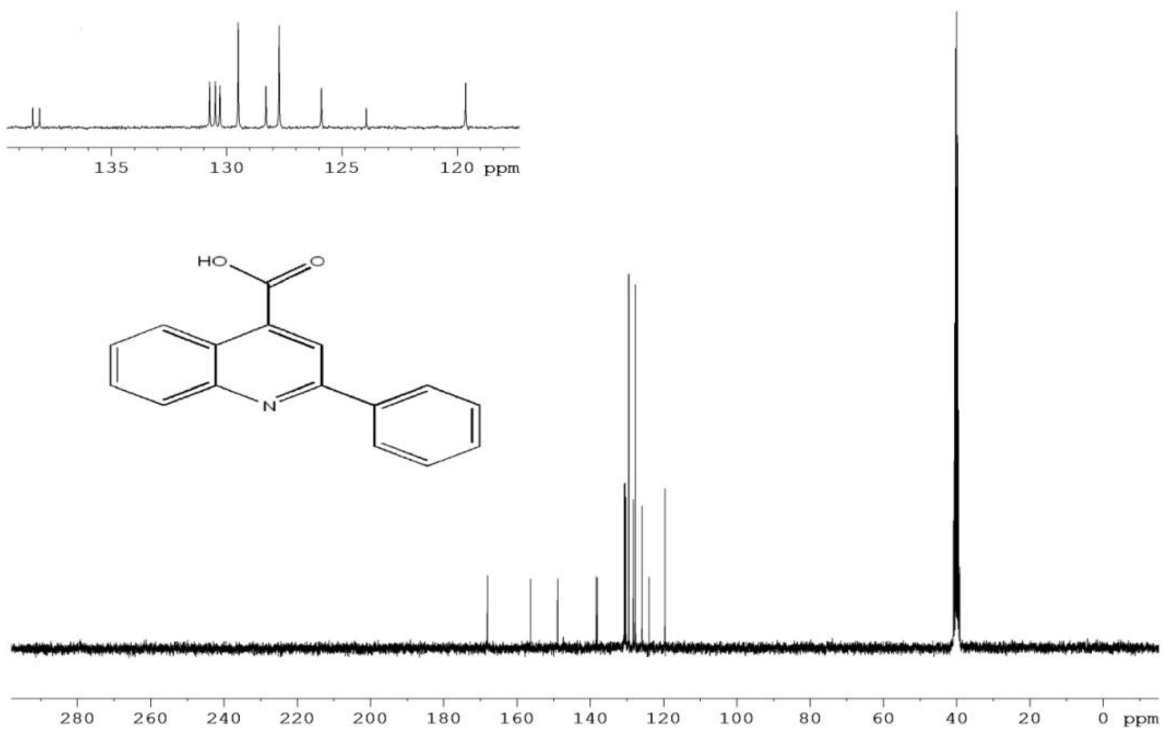


Figure 4. ^{13}C-NMR spectrum of compound [**64a**] (DMSO-d_6).

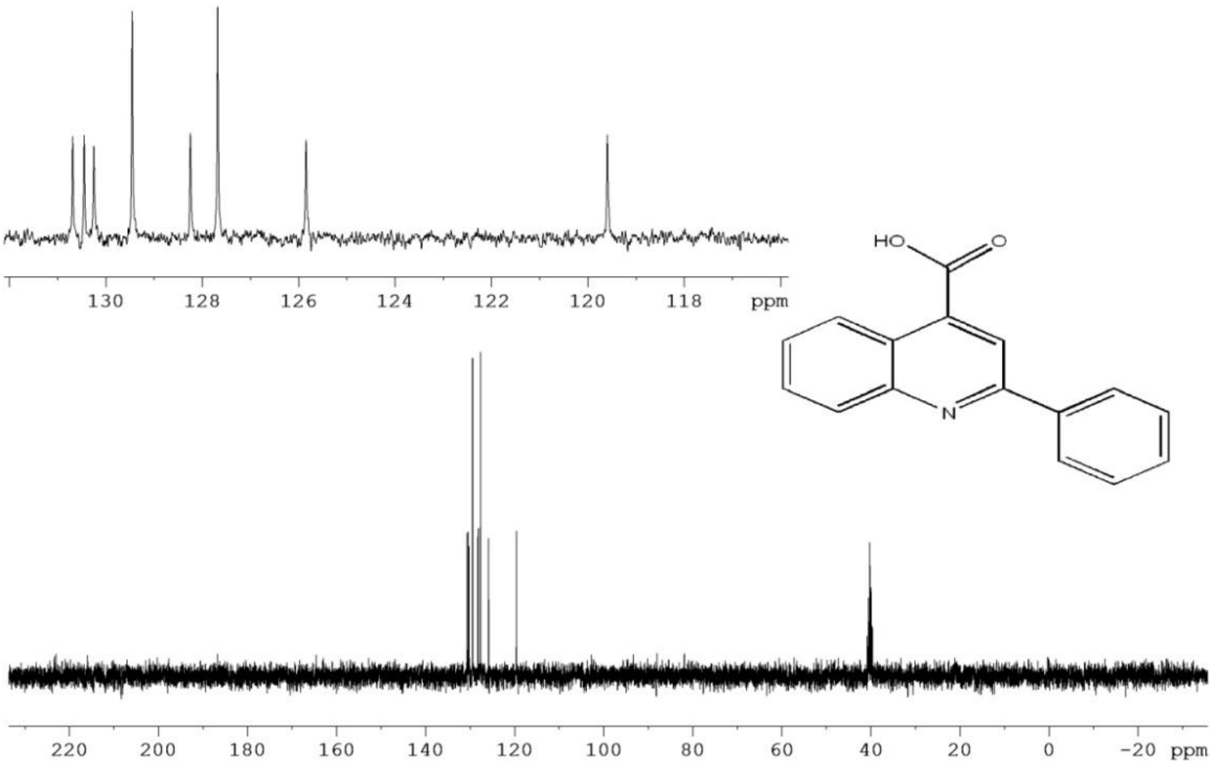


Figure 5. DEPT 135 spectrum of compound [**64a**] (DMSO-d_6).

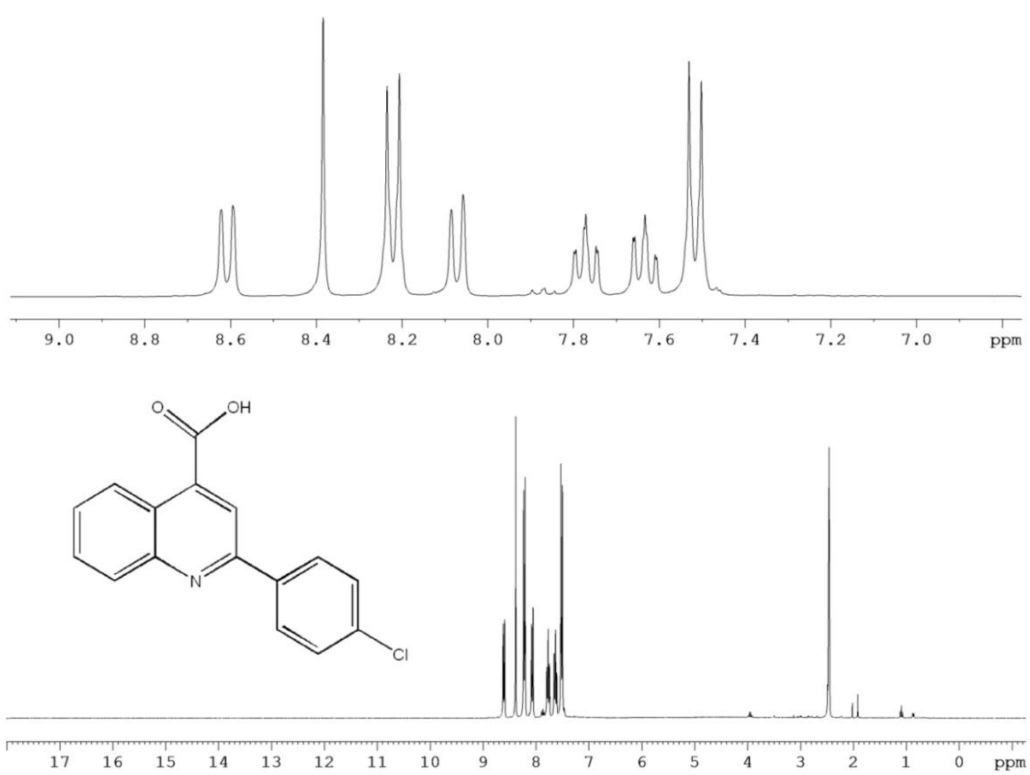


Figure 6. ^{1}H-NMR spectrum of compound [**64b**] (DMSO-d_6).

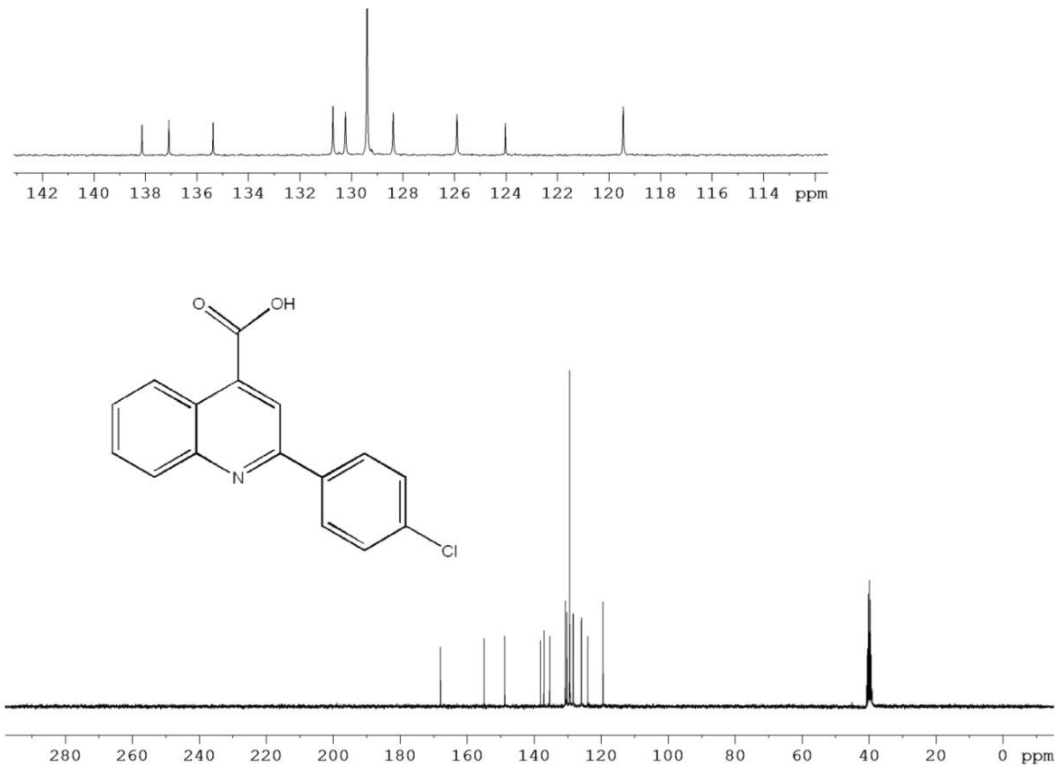


Figure 7. ^{13}C-NMR spectrum of compound [**64b**] (DMSO-d_6).

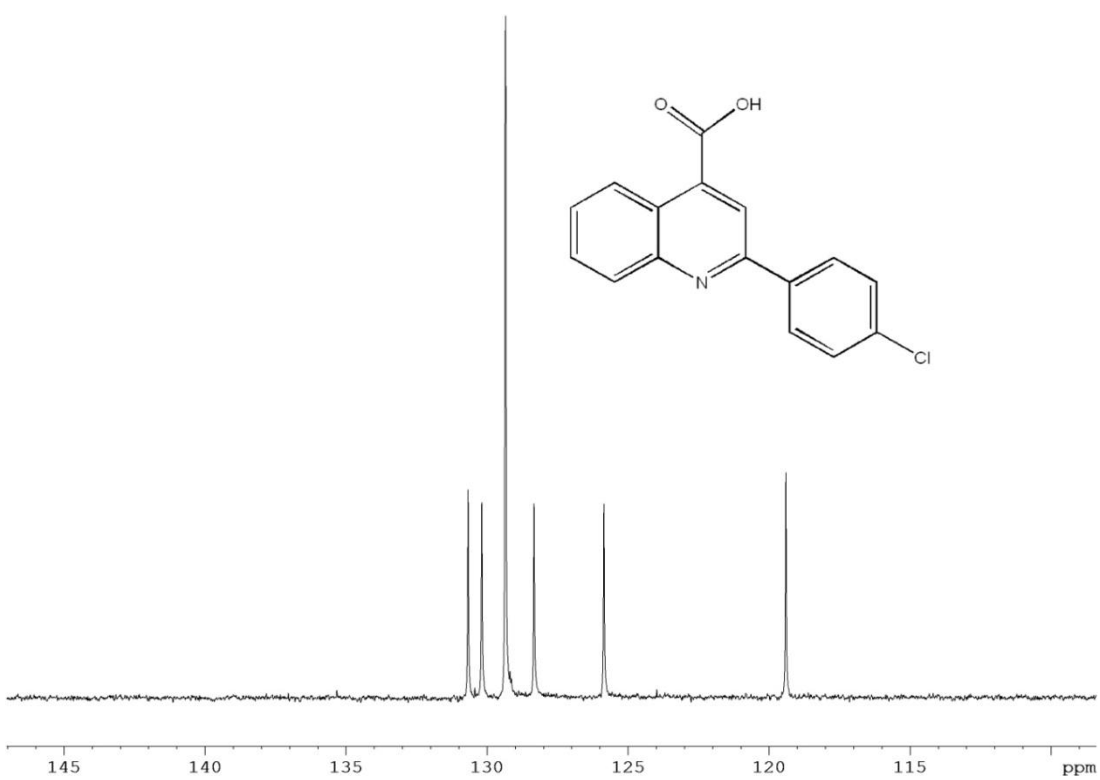


Figure 8. DEPT 135 spectrum of compound [**64b**] (DMSO-d_6).

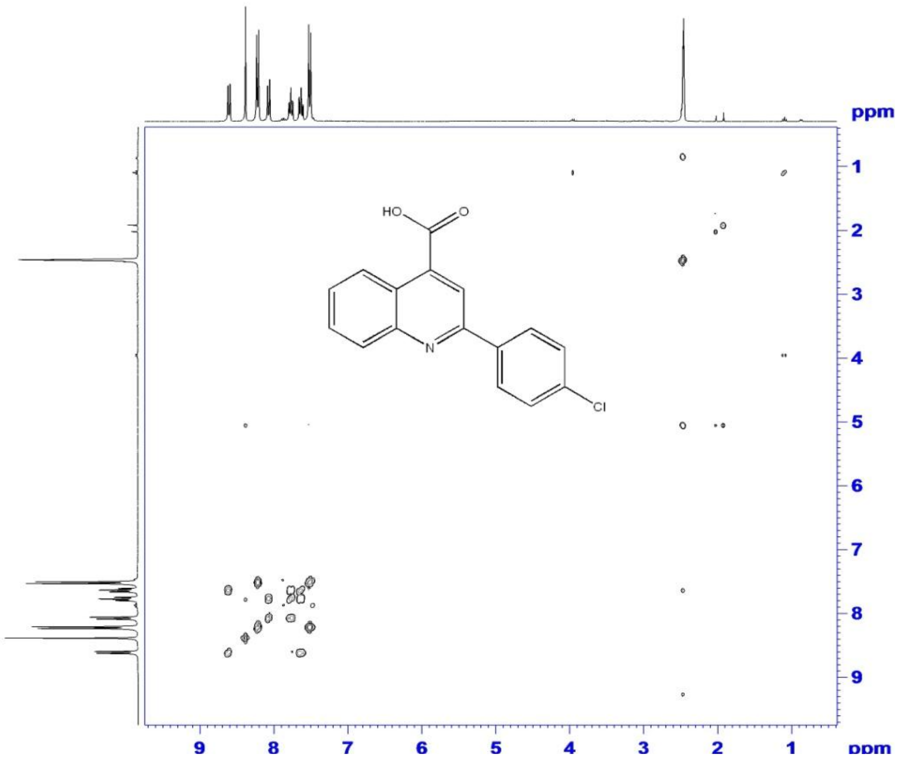


Figure 9. COSY spectrum (1) of compound [64b] **(**DMSO-d_6**).**

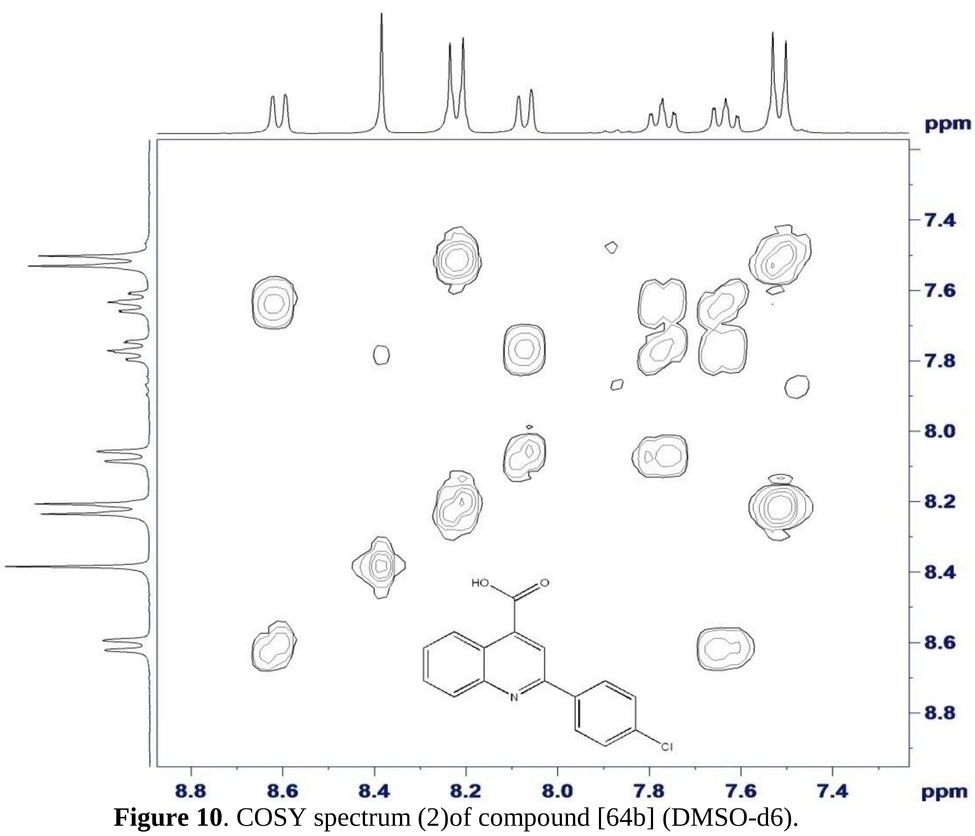


Figure 10. COSY spectrum (2)of compound [64b] (DMSO-d6).

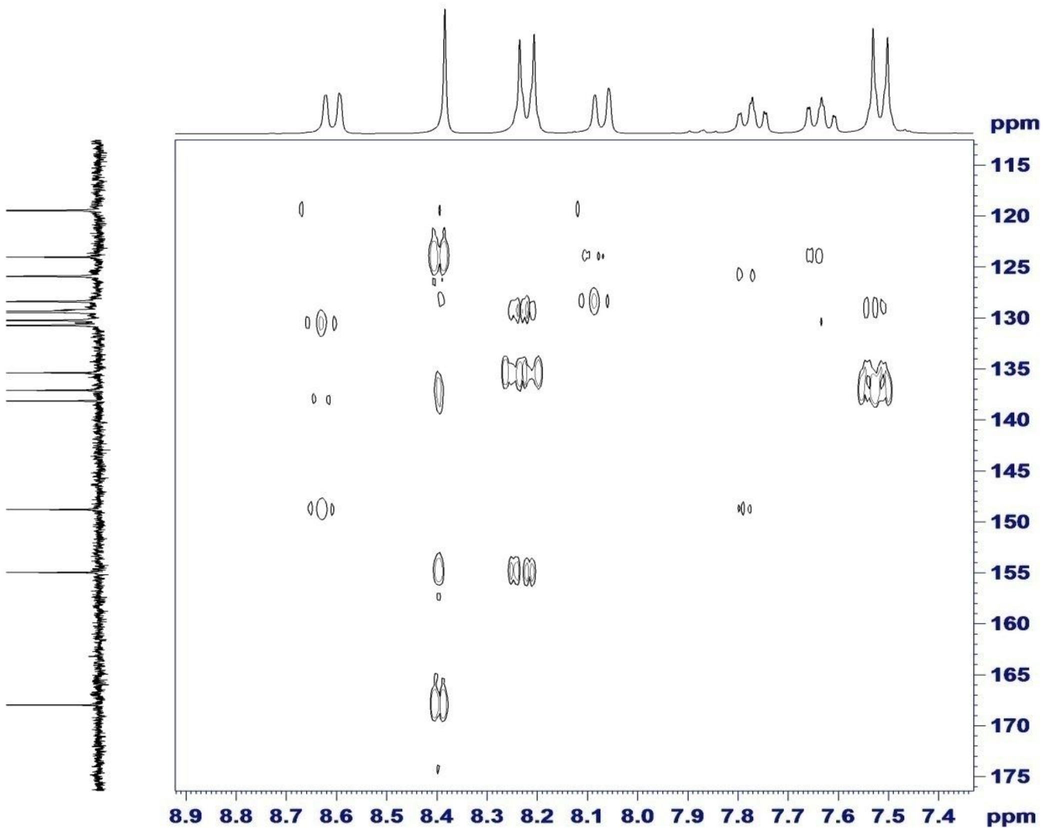


Figure 11. HMBC spectrum of compound **[64b]** (DMSO-d_6).

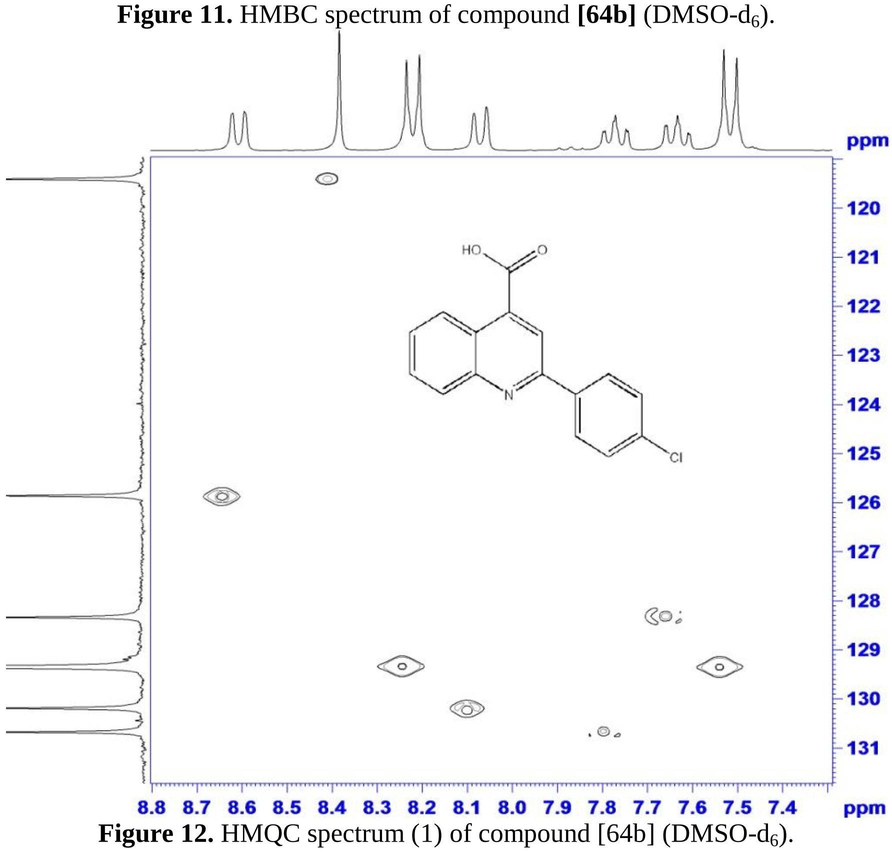


Figure 12. HMQC spectrum (1) of compound [64b] (DMSO-d_6).

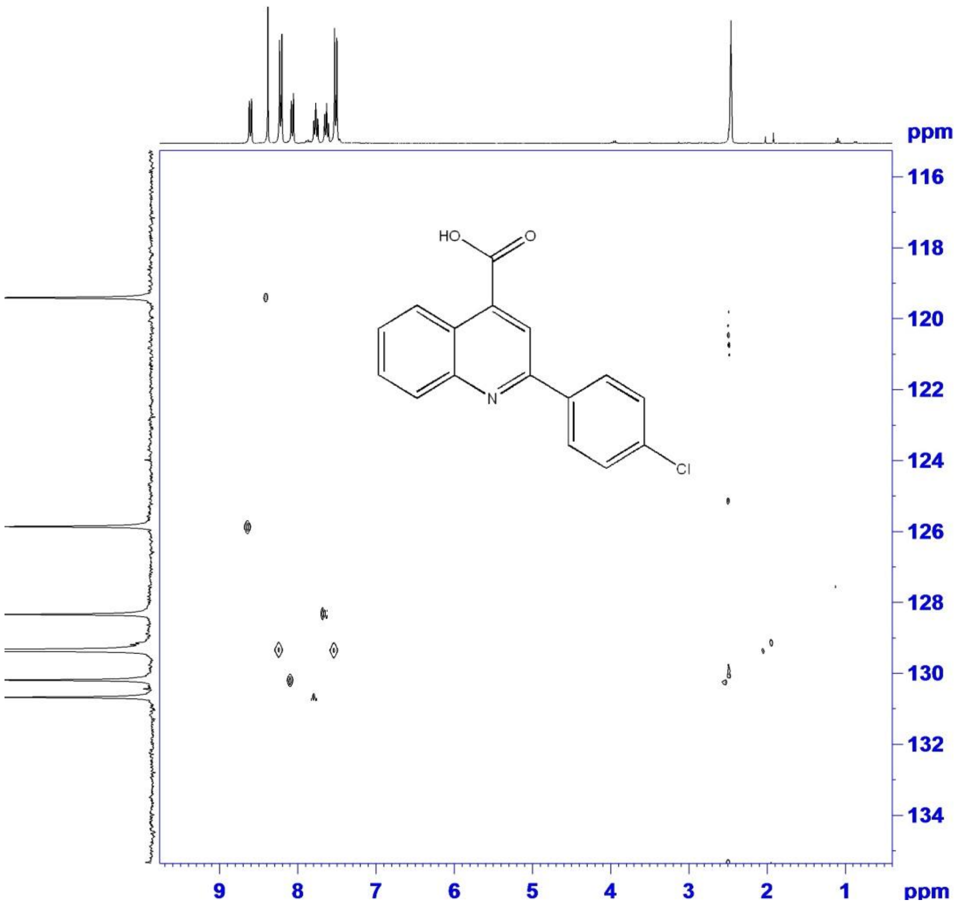


Figure 13. HMQC spectrum (2) of compound [64b] (DMSO-d_6).

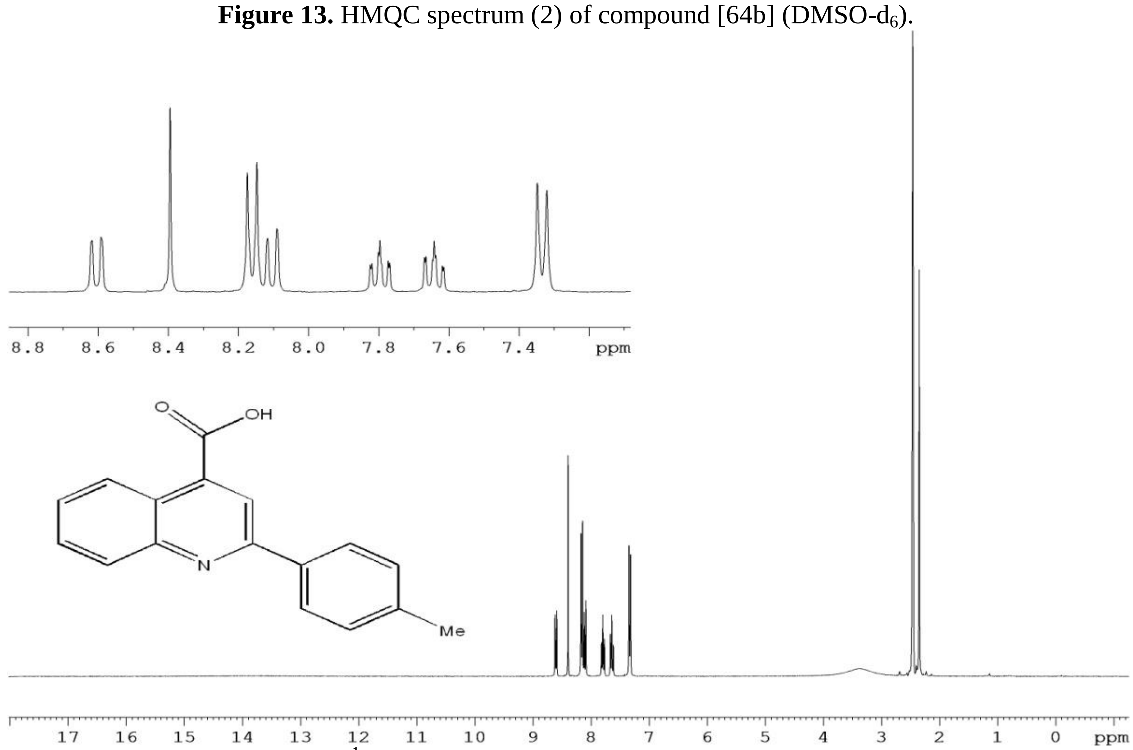


Figure 14. ^{1}H-NMR spectrum of compound [**64c**] (DMSO-d_6).

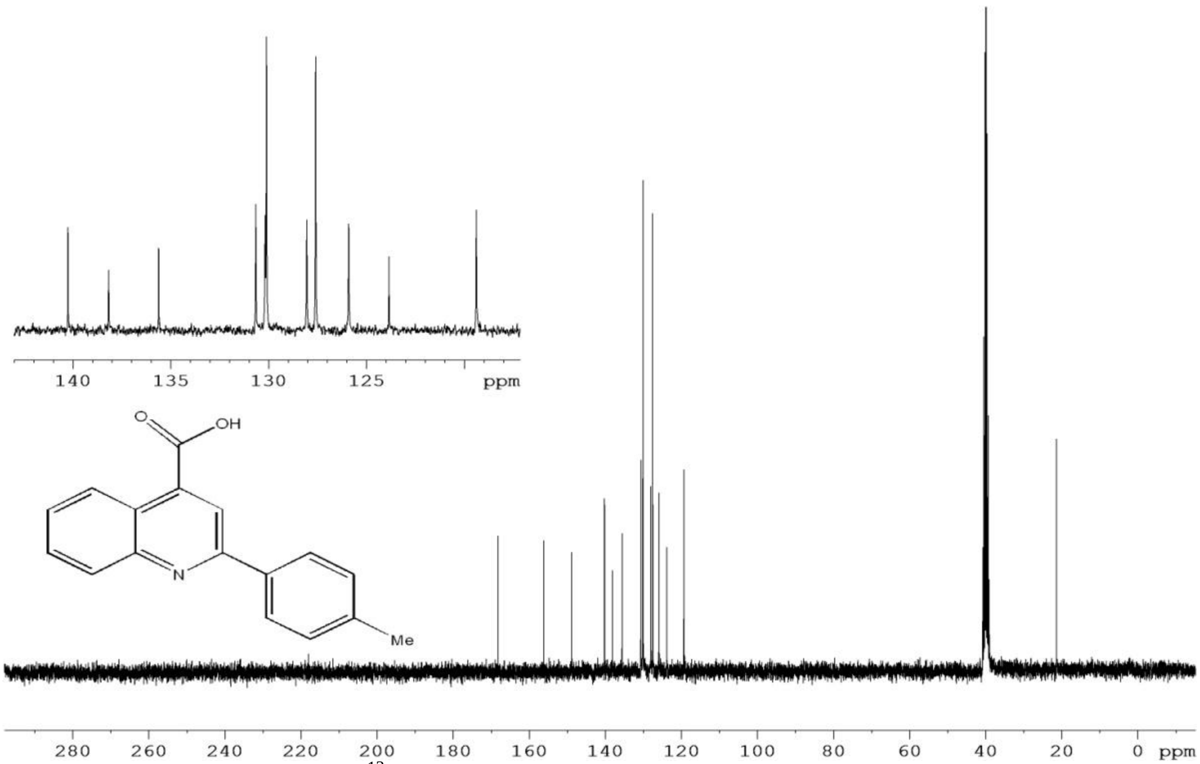


Figure 15. ^{13}C-NMR spectrum of compound [**64c**] (DMSO-d_6).

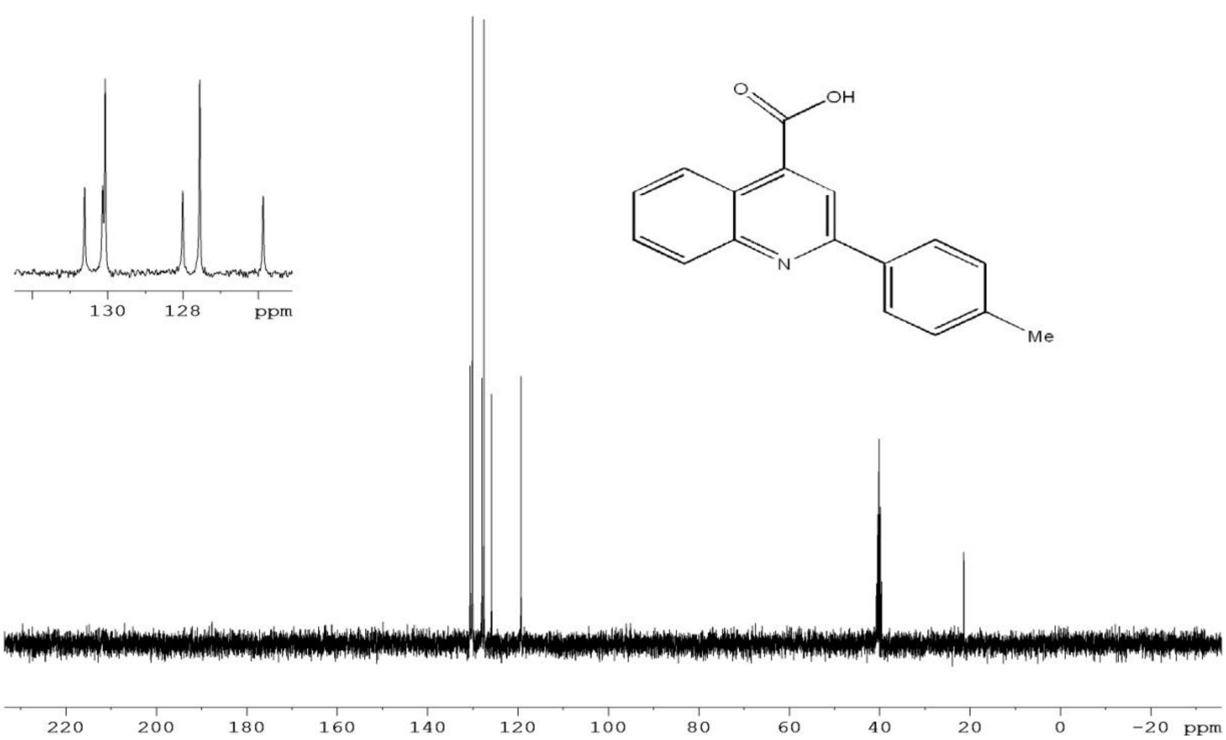


Figure 16. DEPT 135 spectrum of compound [**64c**] (DMSO-d_6).

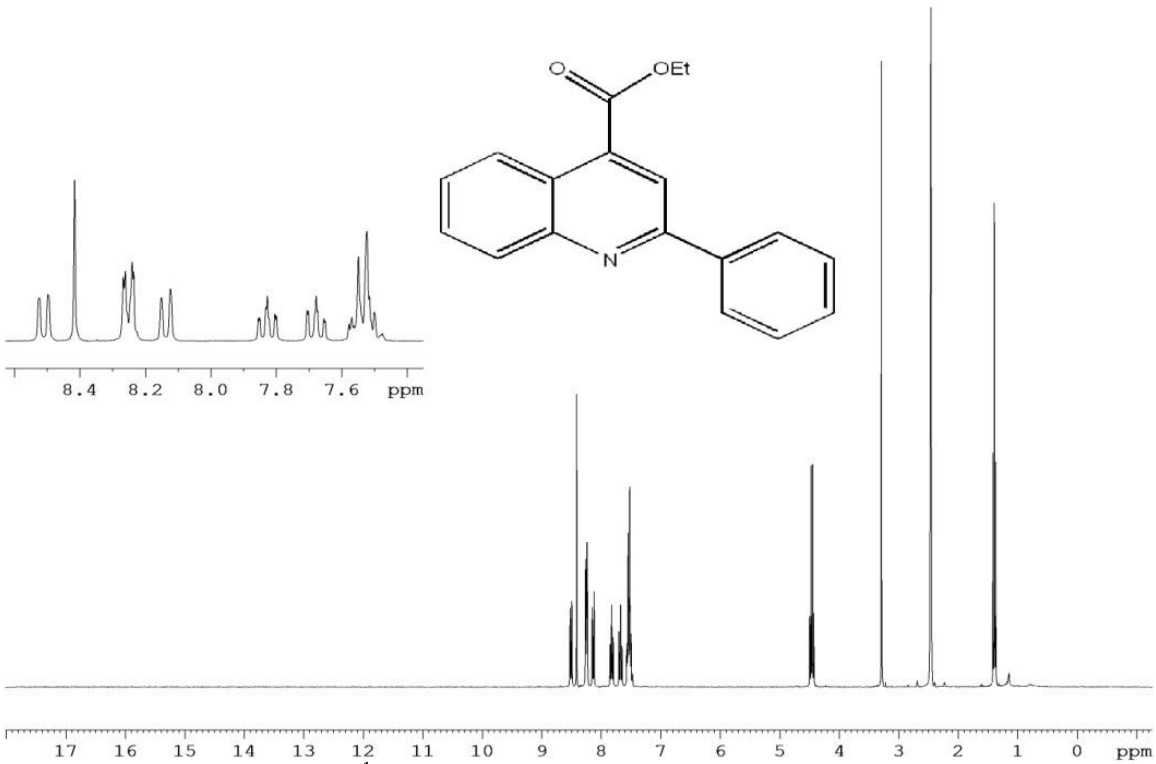


Figure 17. ^{1}H-NMR spectrum of compound [**65a**] (DMSO-d_6).

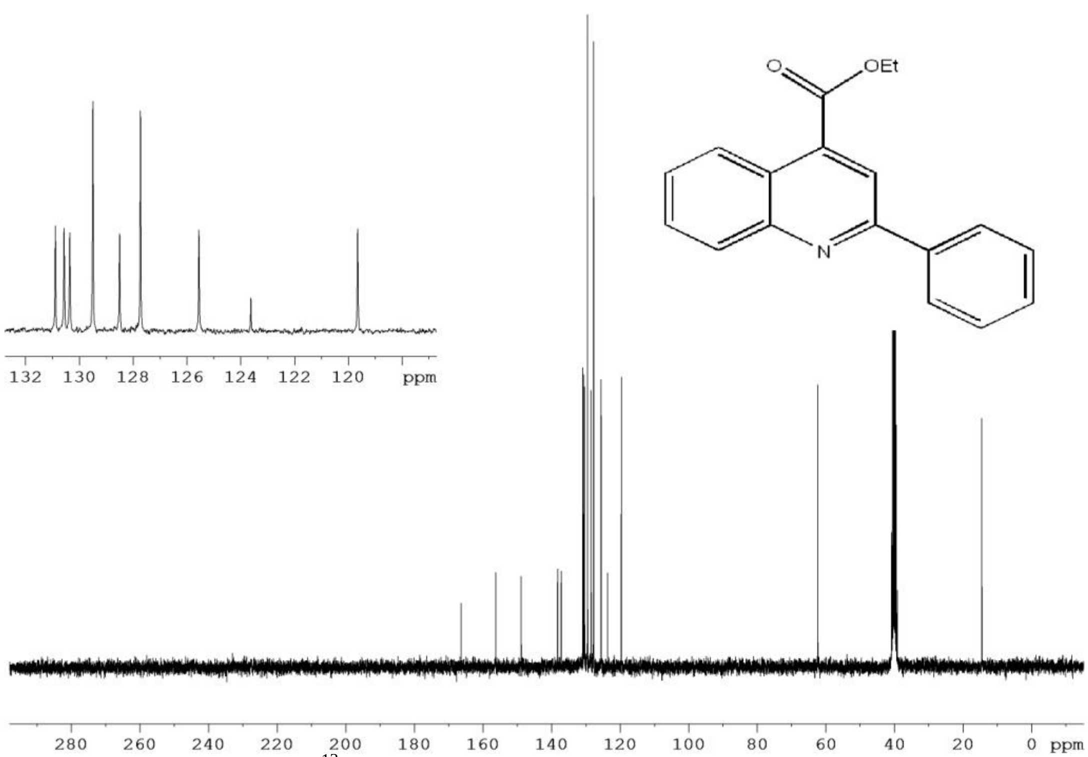


Figure 18. ^{13}C-NMR spectrum of compound [**65a**] (DMSO-d_6).

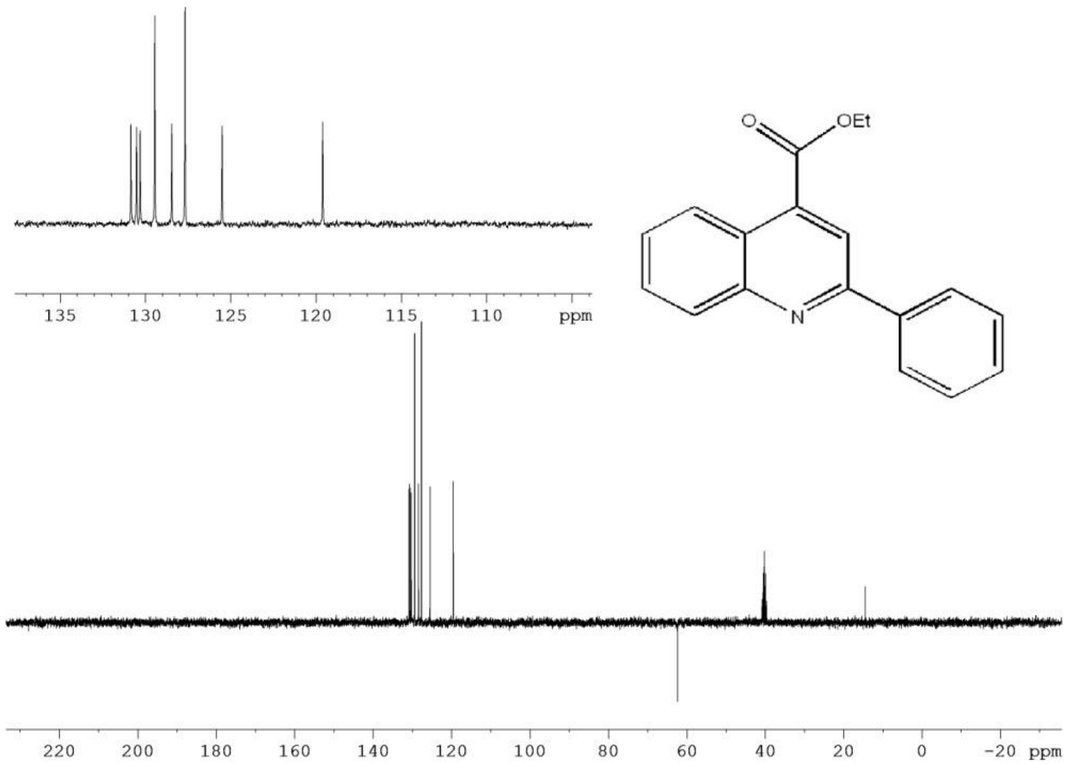


Figure 19. DEPT 135 spectrum of compound [**65a**] (DMSO-d_6).

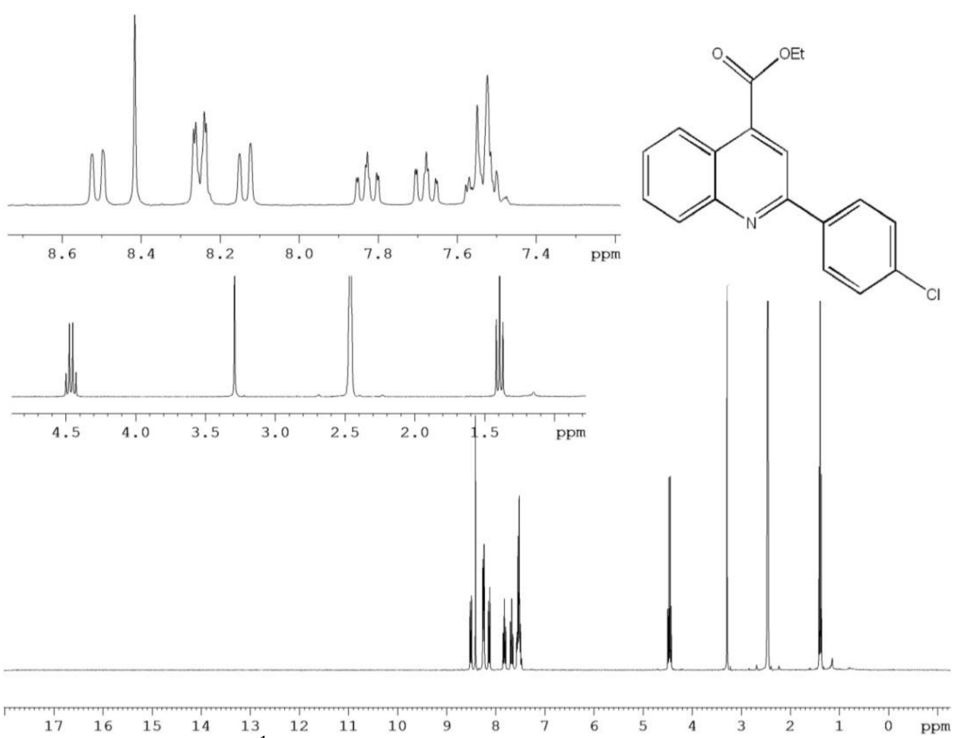


Figure 20. ^{1}H-NMR spectrum of compound [**65b**] (DMSO-d_6).

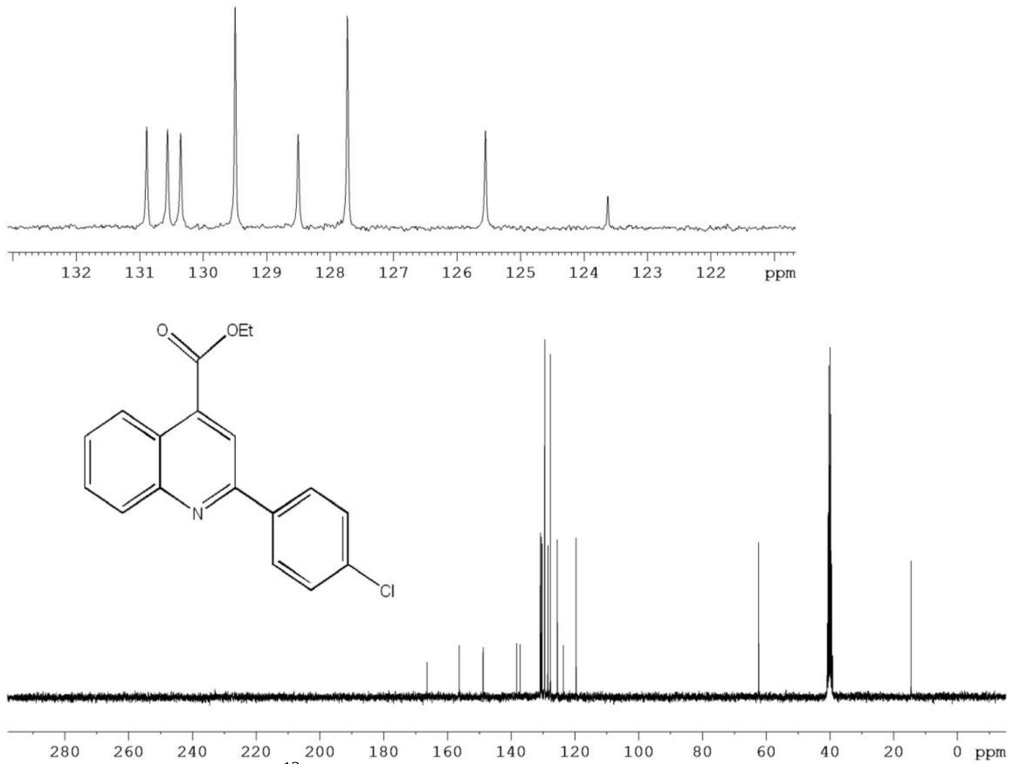


Figure 21. ^{13}C-NMR spectrum of compound [**65b**] (DMSO-d_6).

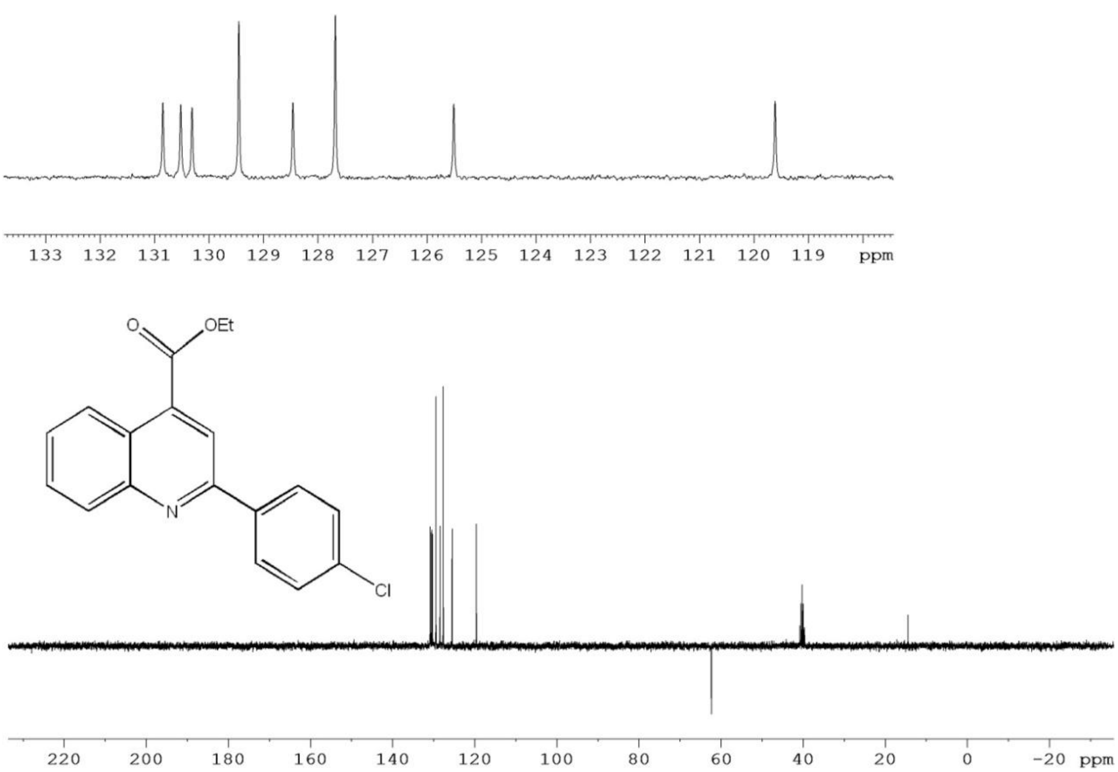


Figure 22. DEPT 135 spectrum of compound [**65b**] (DMSO-d_6).

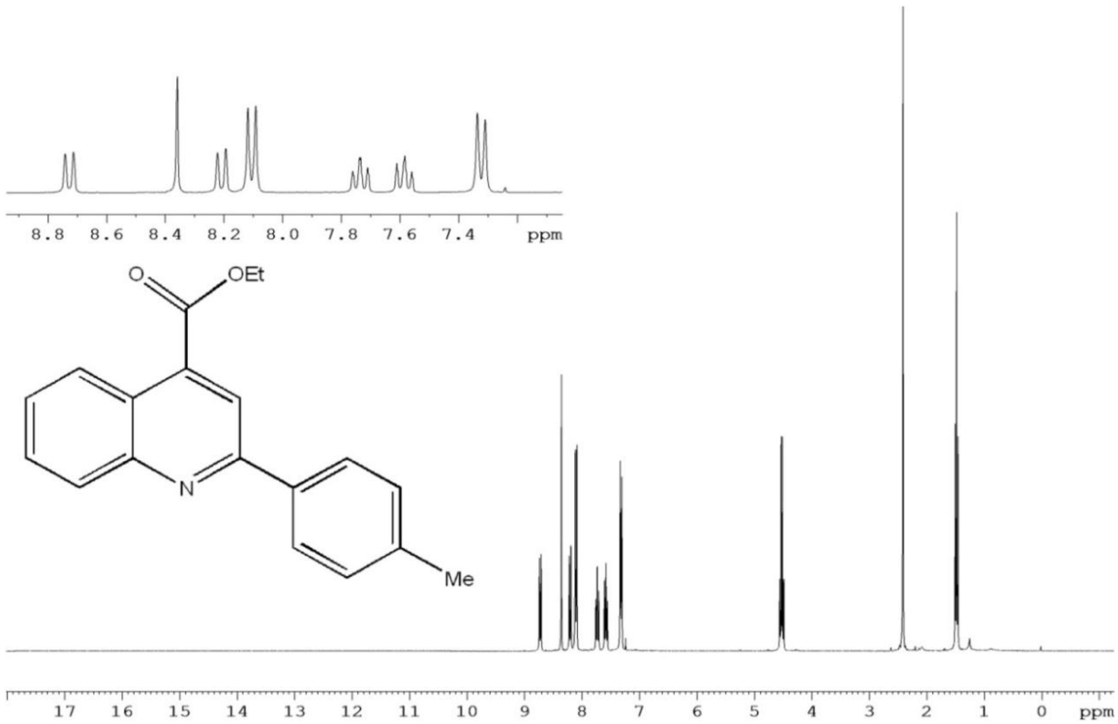


Figure 23. ^{1}H-NMR spectrum of compound [**65c**] ($CDCl_3$).

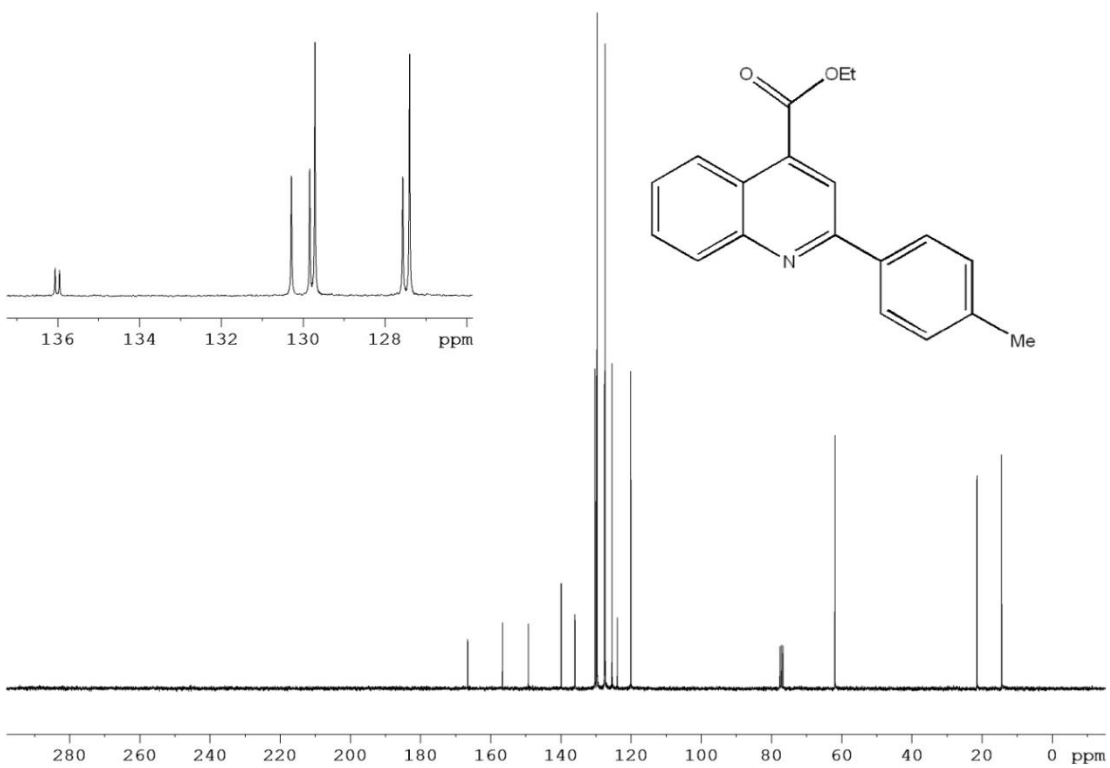


Figure 24. ^{13}C-NMR spectrum of compound [**65c**] ($CDCl_3$).

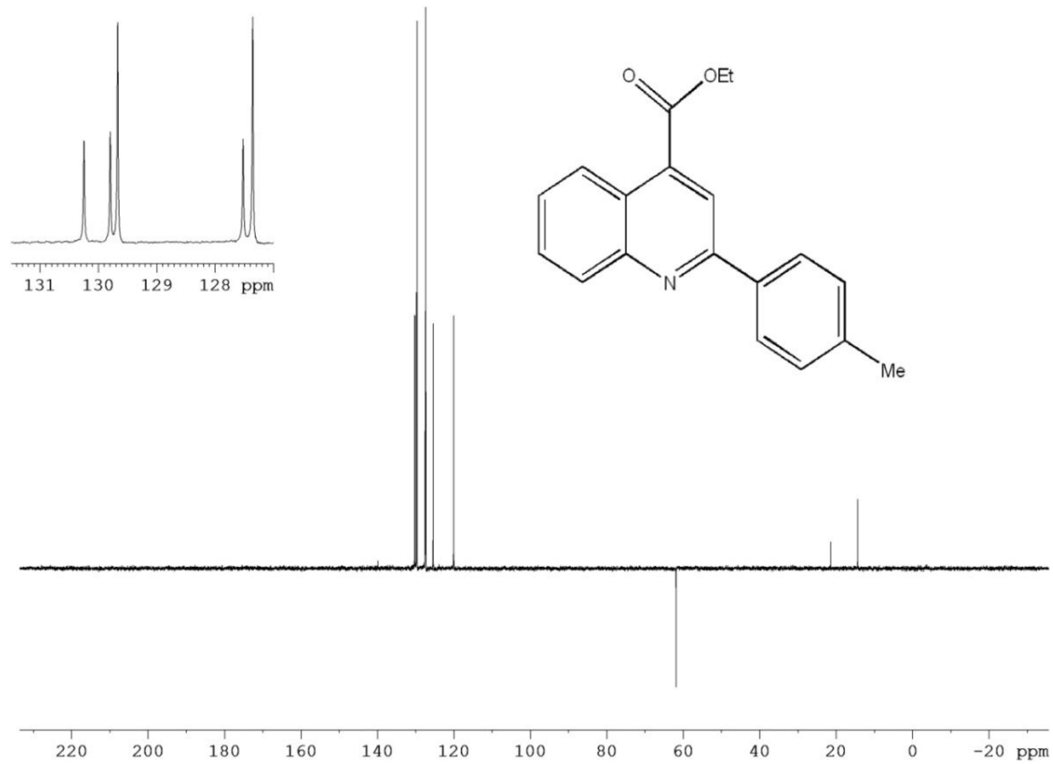


Figure 25. DEPT 135 spectrum of compound [65c] ($CDCl_3$).

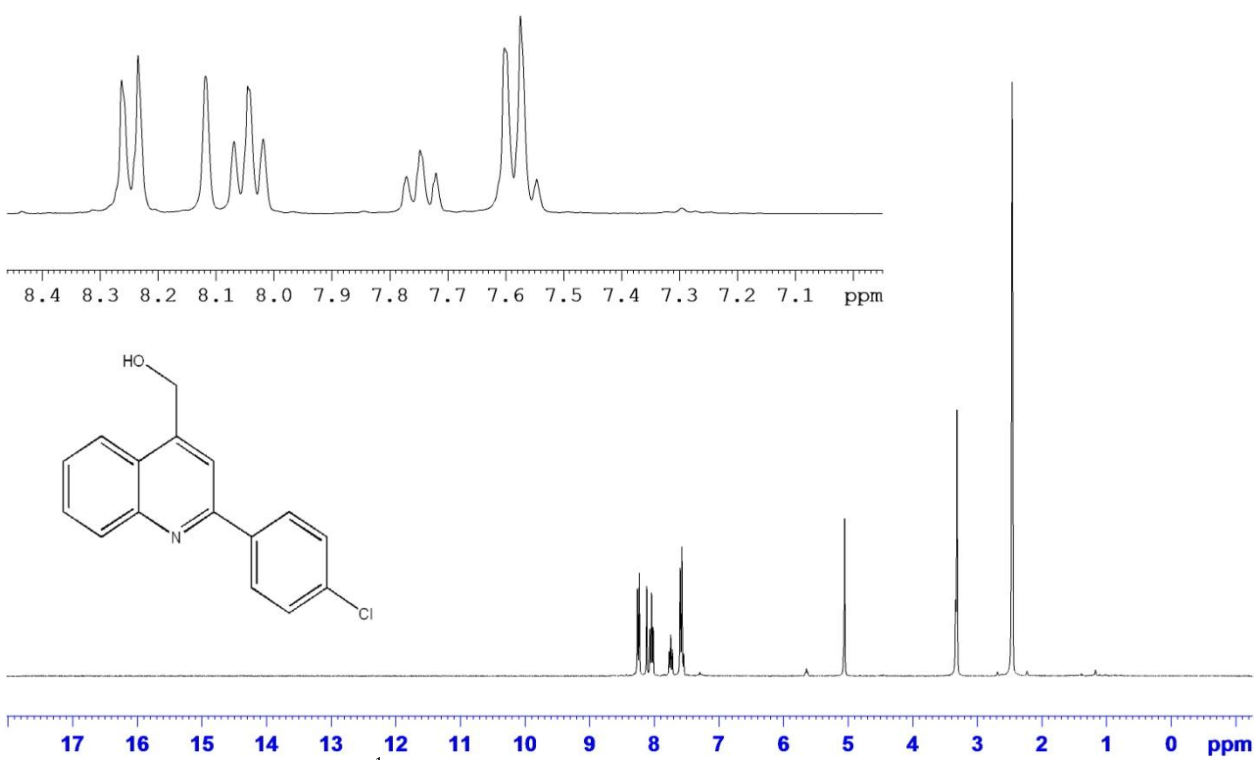


Figure 26. ^{1}H-NMR spectrum of compound **[66b]** (DMSO-d_6).

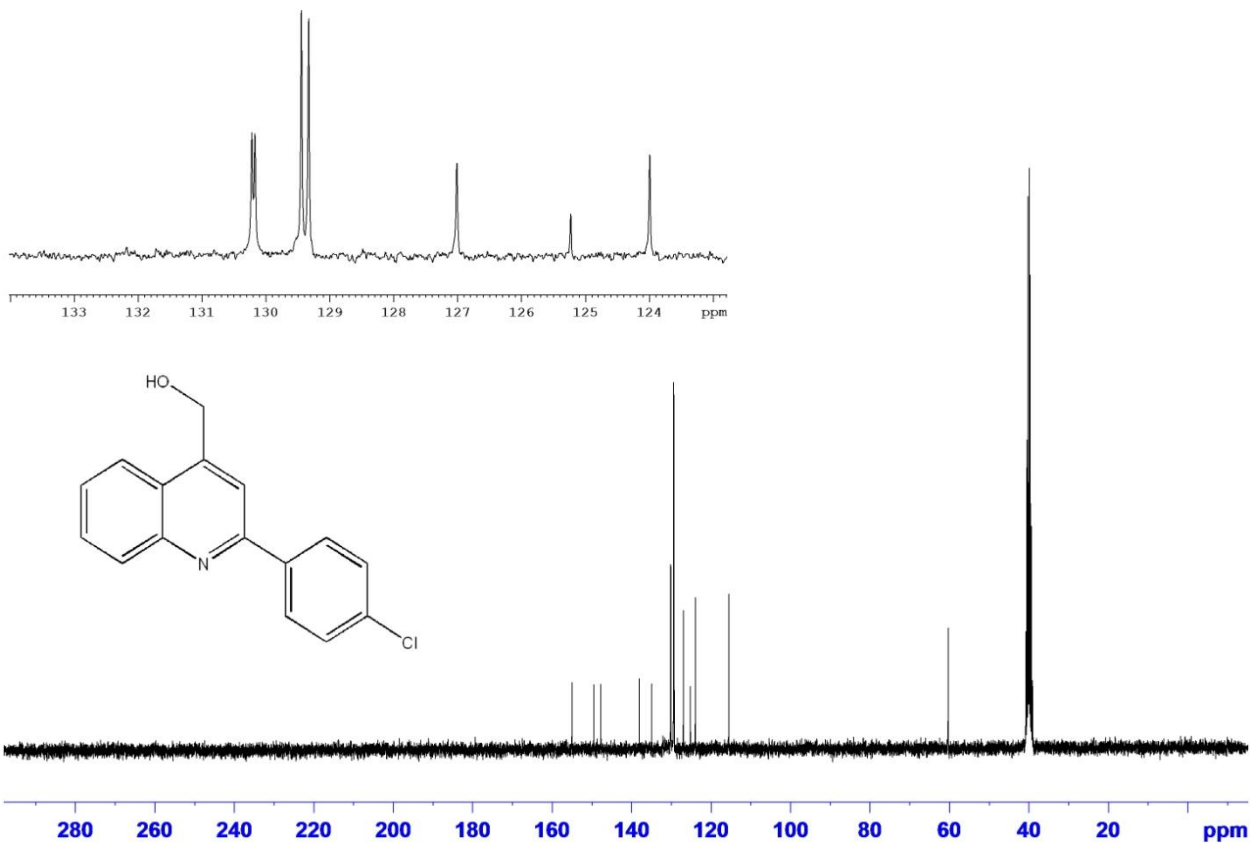


Figure 27. 13 C-NMR spectrum of compound [66b] (DMSO-d_6).

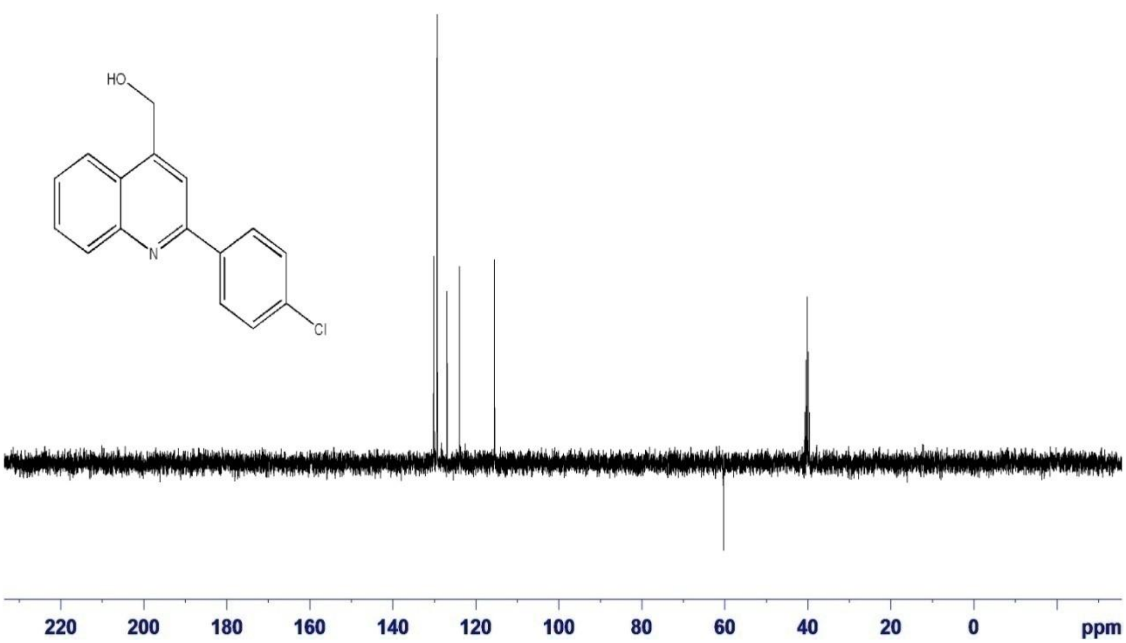


Figure 28. DEPT 135 spectrum of compound [66b] (DMSO-d_6).

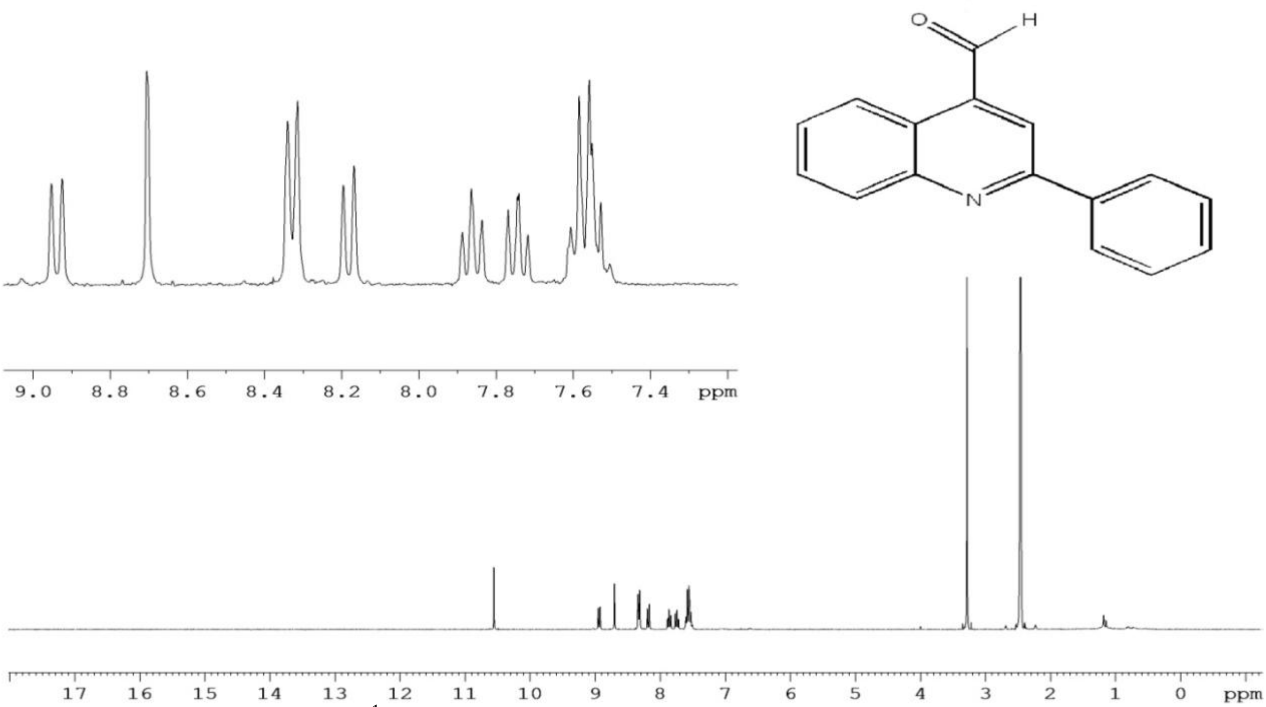


Figure 29. ^{1}H-NMR spectrum of compound **[67a]** (DMSO-d_6).

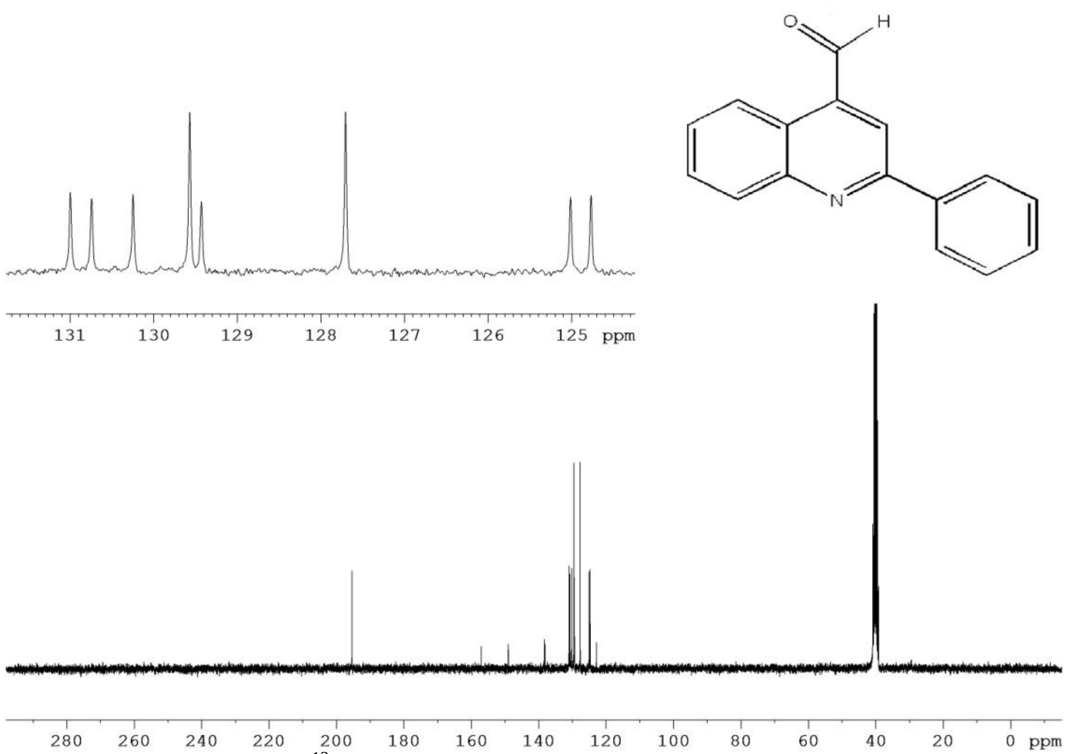


Figure 30. ^{13}C-NMR spectrum of compound **[67a]** (DMSO-d_6).

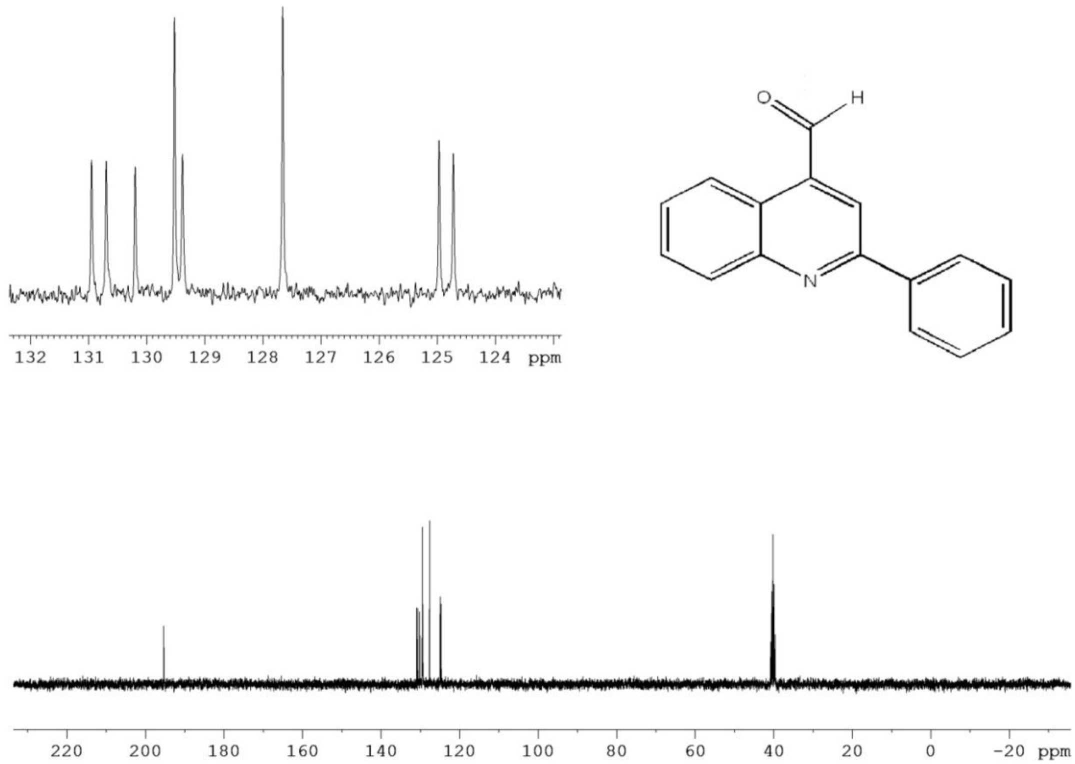


Figure 31. DEPT 135 spectrum of compound **[67a**] (DMSO-d_6).

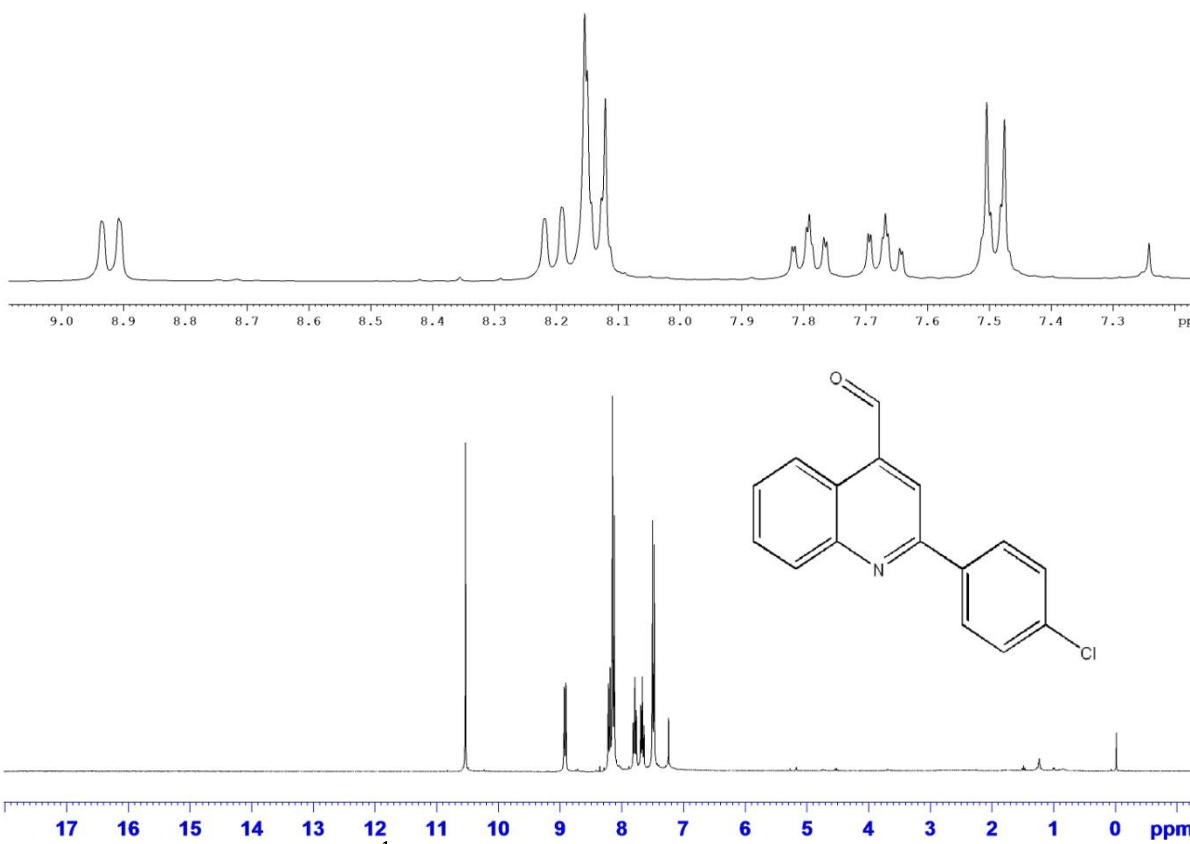


Figure 32. ^{1}H-NMR spectrum of compound [67b] ($CDCl_3$).

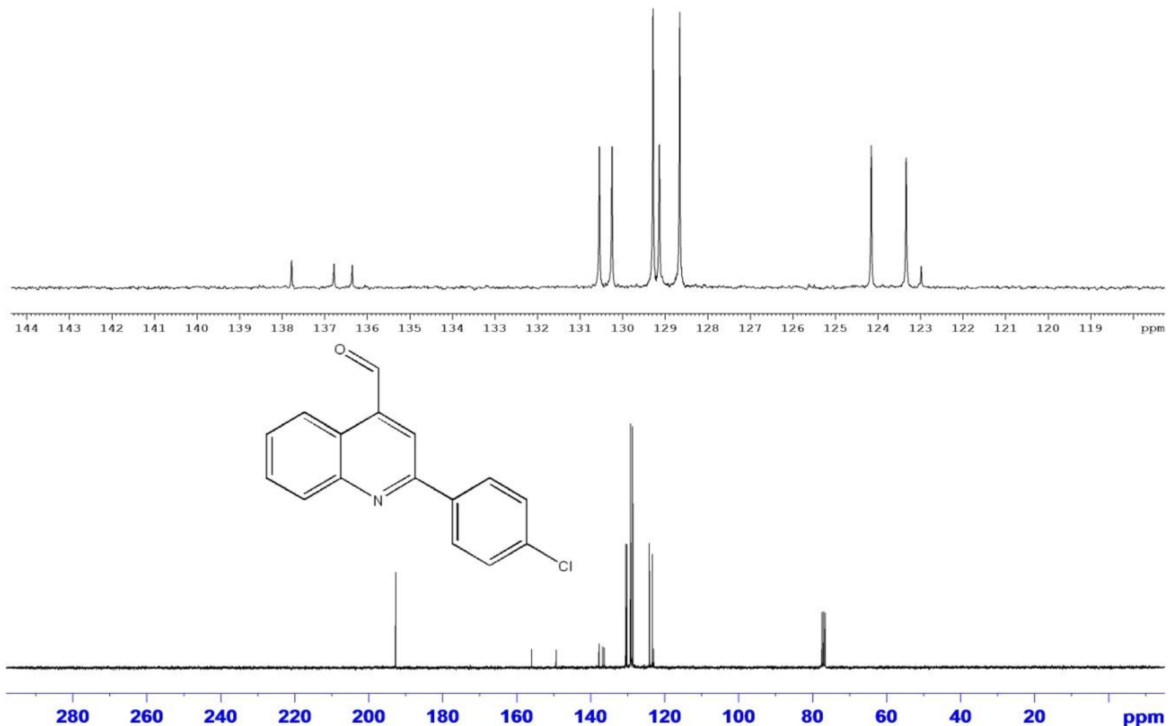


Figure 33. ^{13}C-NMR spectrum of compound **[67b**] ($CDCl_3$).

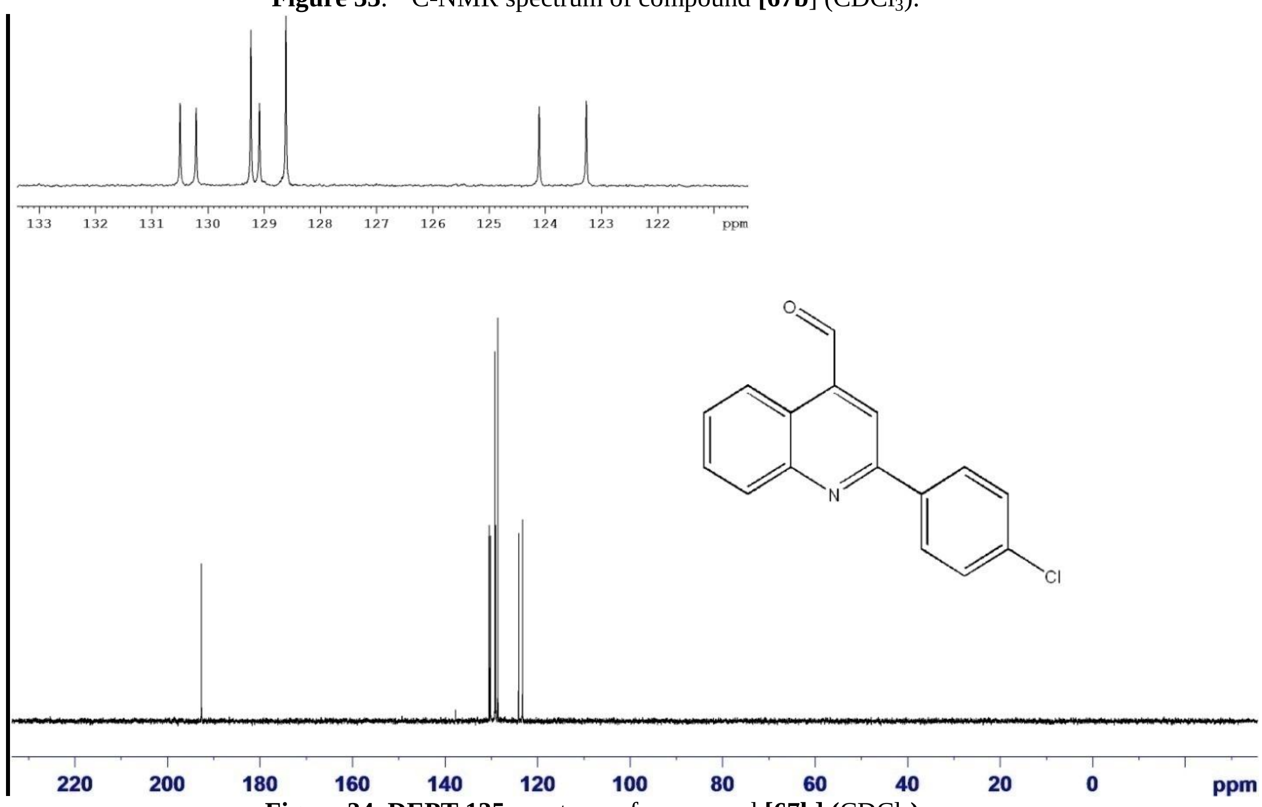


Figure 34. DEPT 135 spectrum of compound **[67b] (**$CDCl_3$**).**

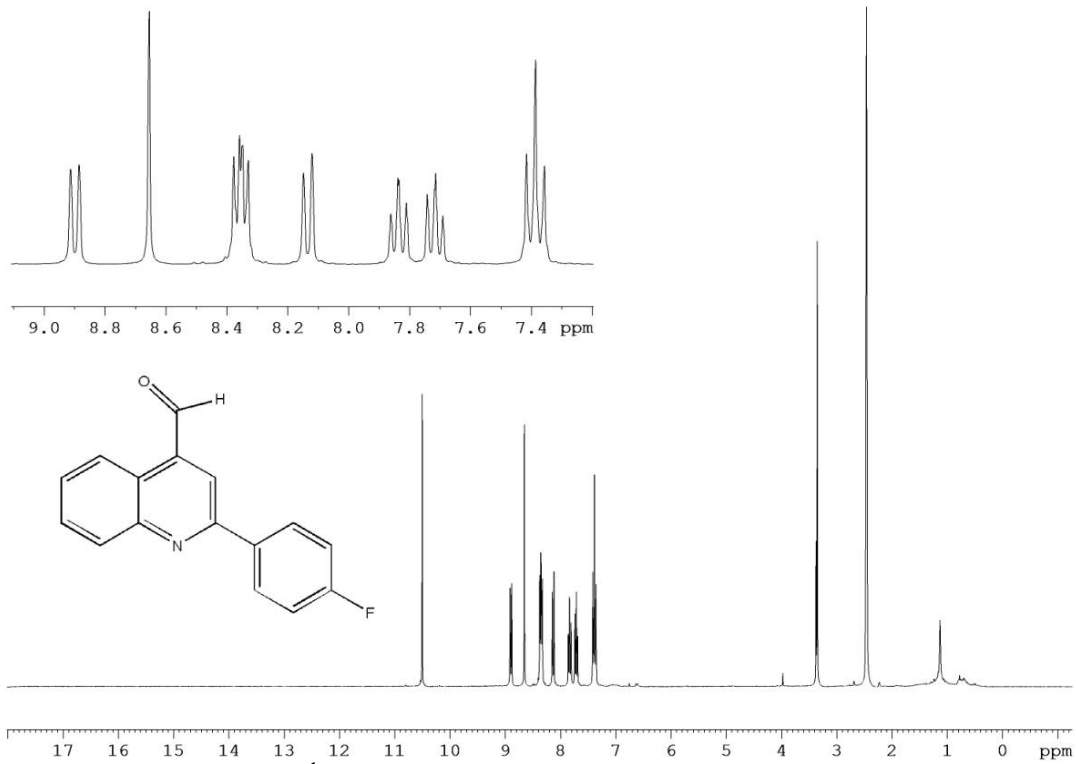


Figure 35. ^{1}H-NMR spectrum of compound [67d] (DMSO-d$_6$).

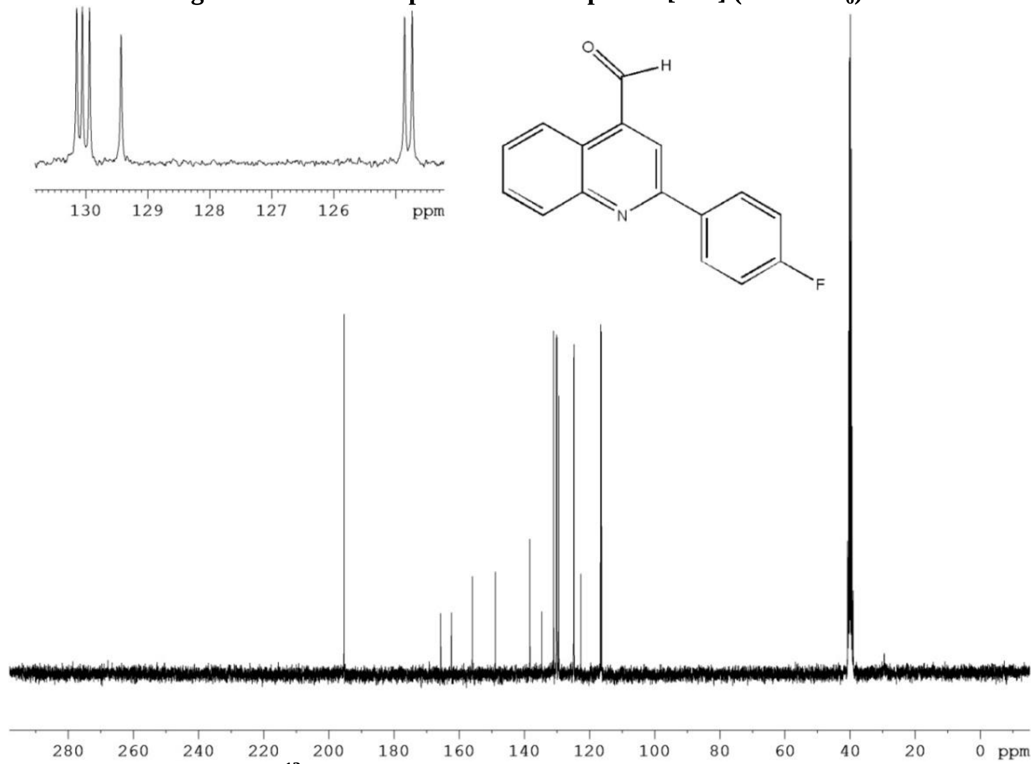


Figure 36. ^{13}C-NMR spectrum of compound [67d] (DMSO-d$_6$).

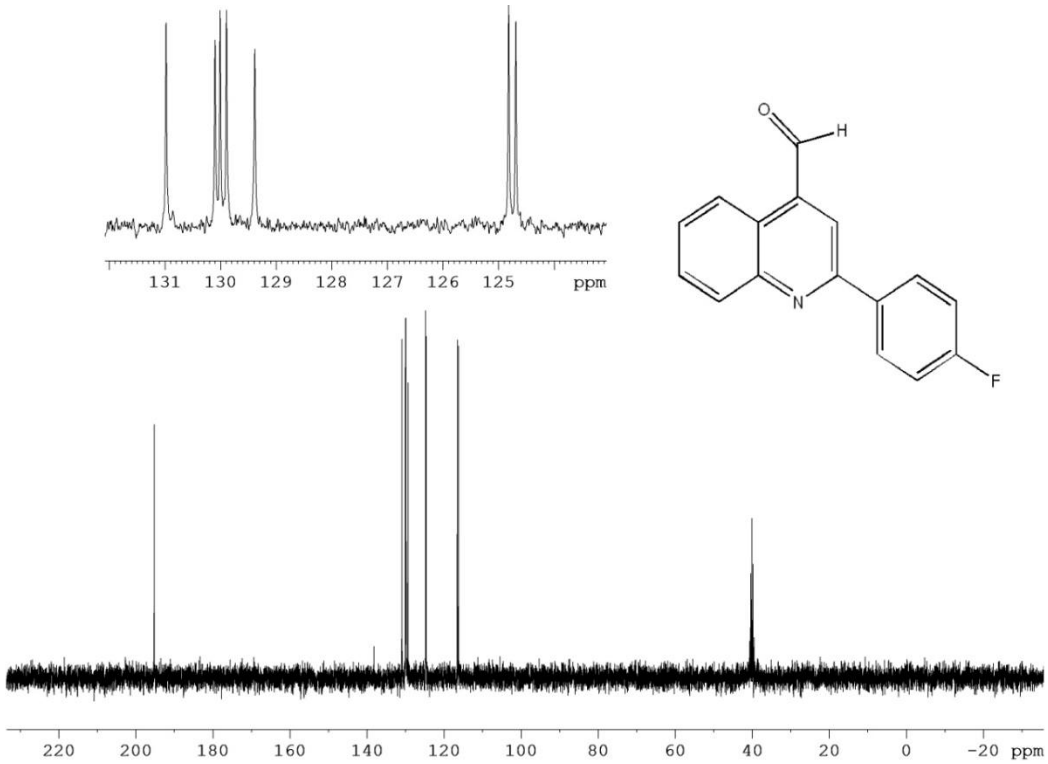


Figure 37. DEPT 135 spectrum of compound [67d] (DMSO-d_6).

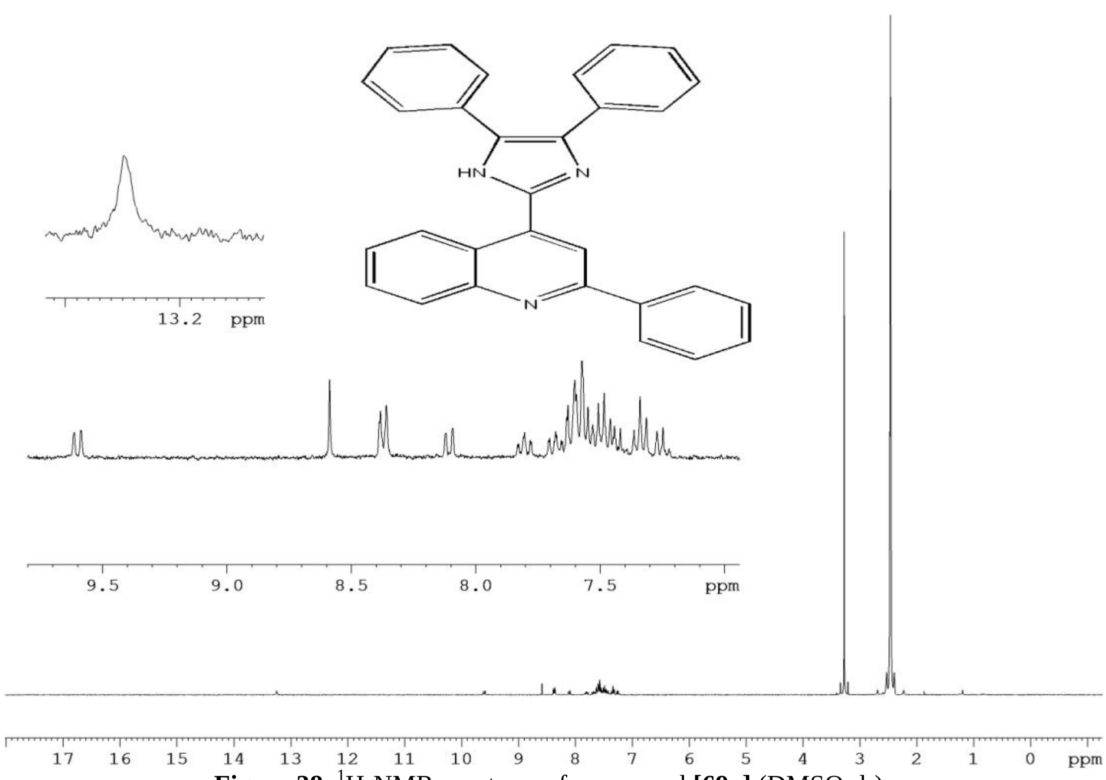


Figure 38. ^{1}H-NMR spectrum of compound **[69a]** (DMSO-d_6).

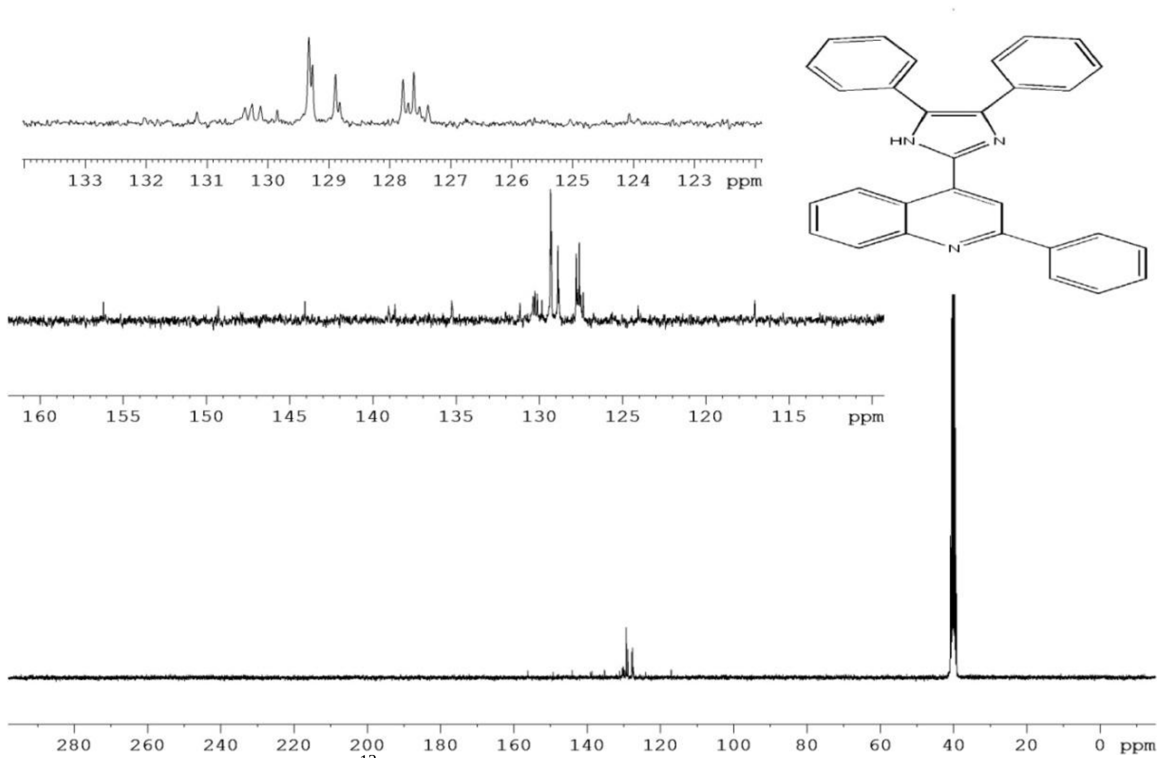


Figure 39. ^{13}C-NMR spectrum of compound **[69a]** (DMSO-d_6).

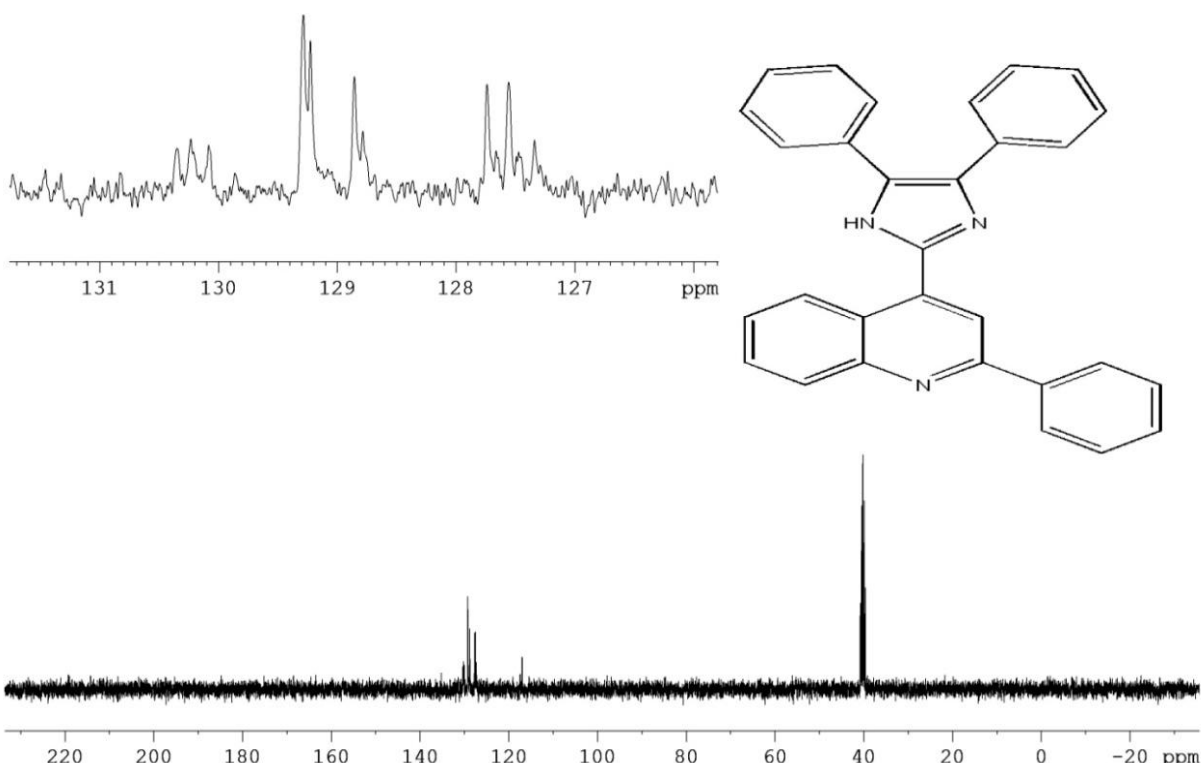


Figure 40. DEPT 135 spectrum of compound [69a] (DMSO-d_6).

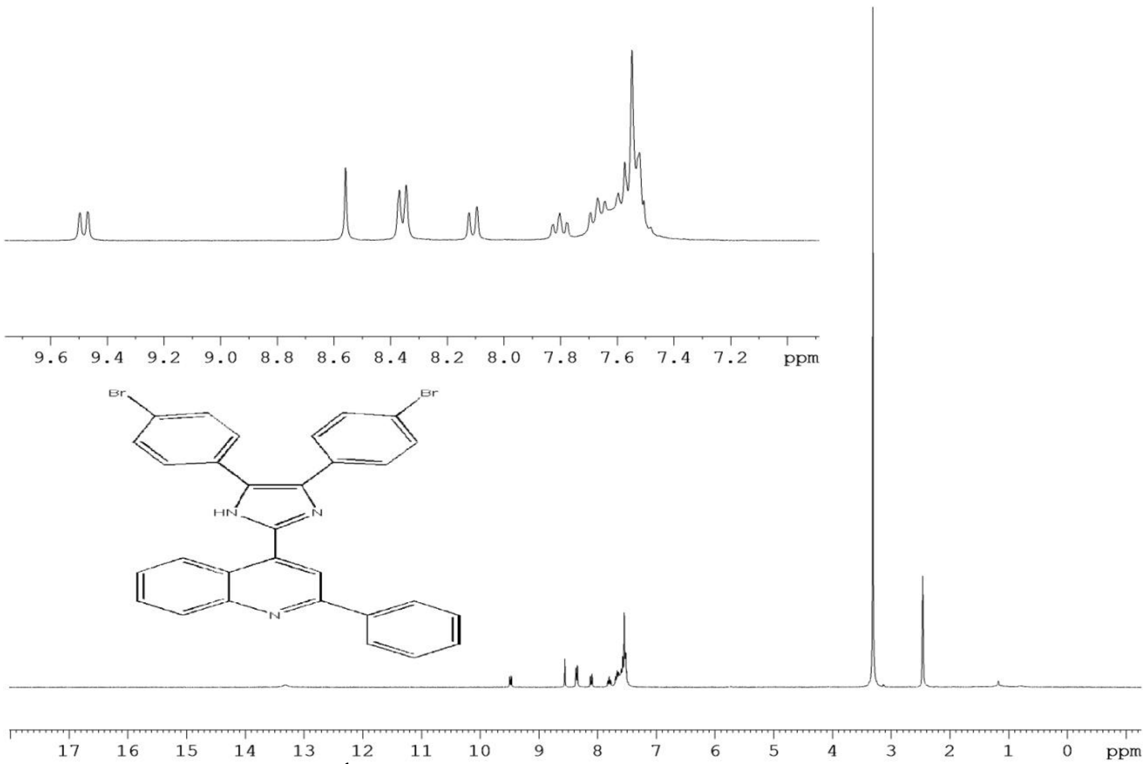


Figure 41. ^{1}H-NMR spectrum of compound [69b] (DMSO-d$_6$).

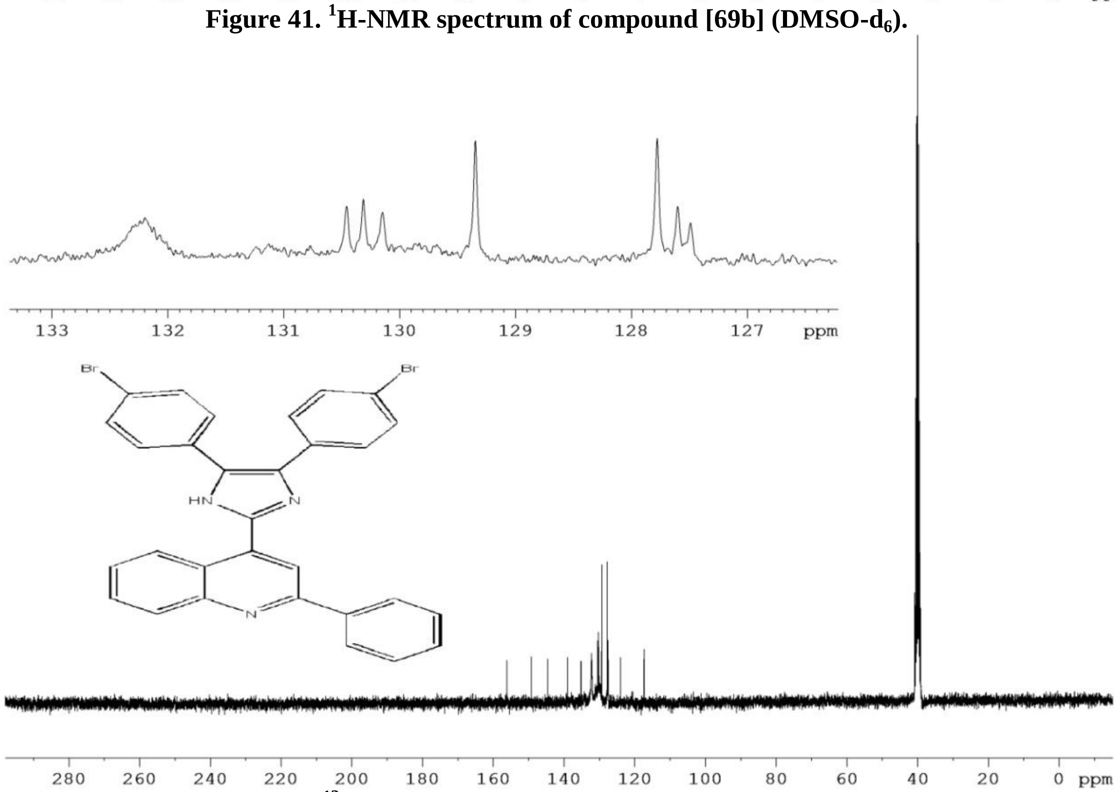


Figure 42. ^{13}C-NMR spectrum of compound [69b] (DMSO-d$_6$).

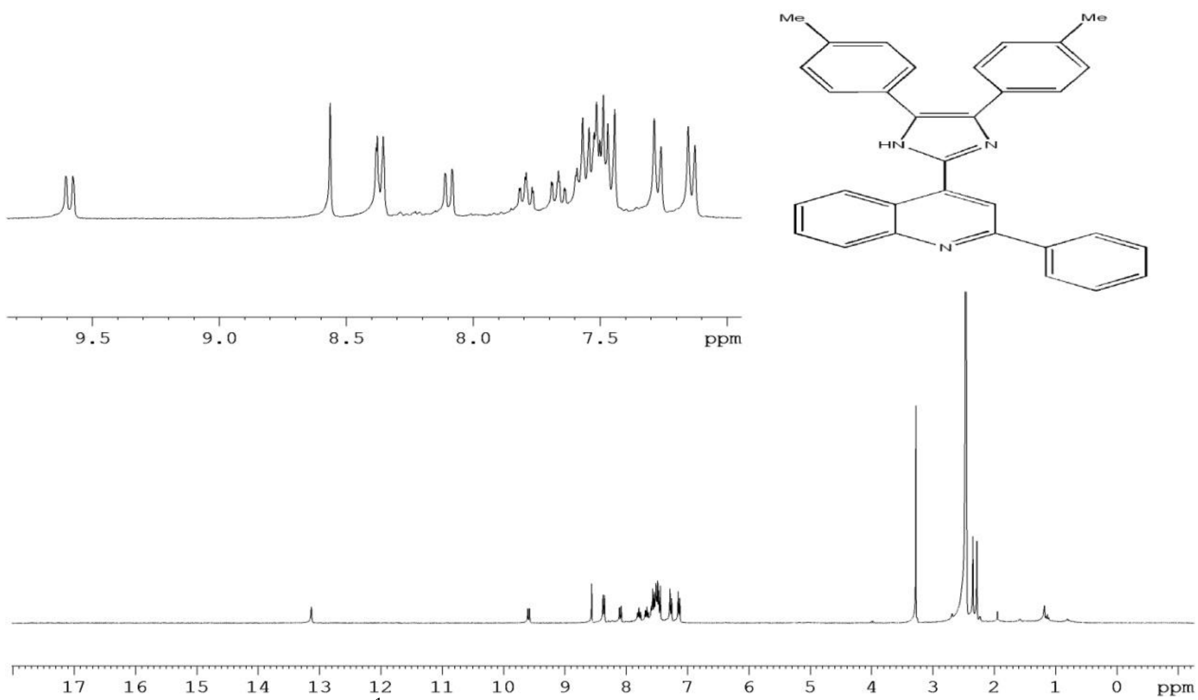


Figure 43. ^{1}H-NMR spectrum of compound **[69d]** (DMSO-d_6).

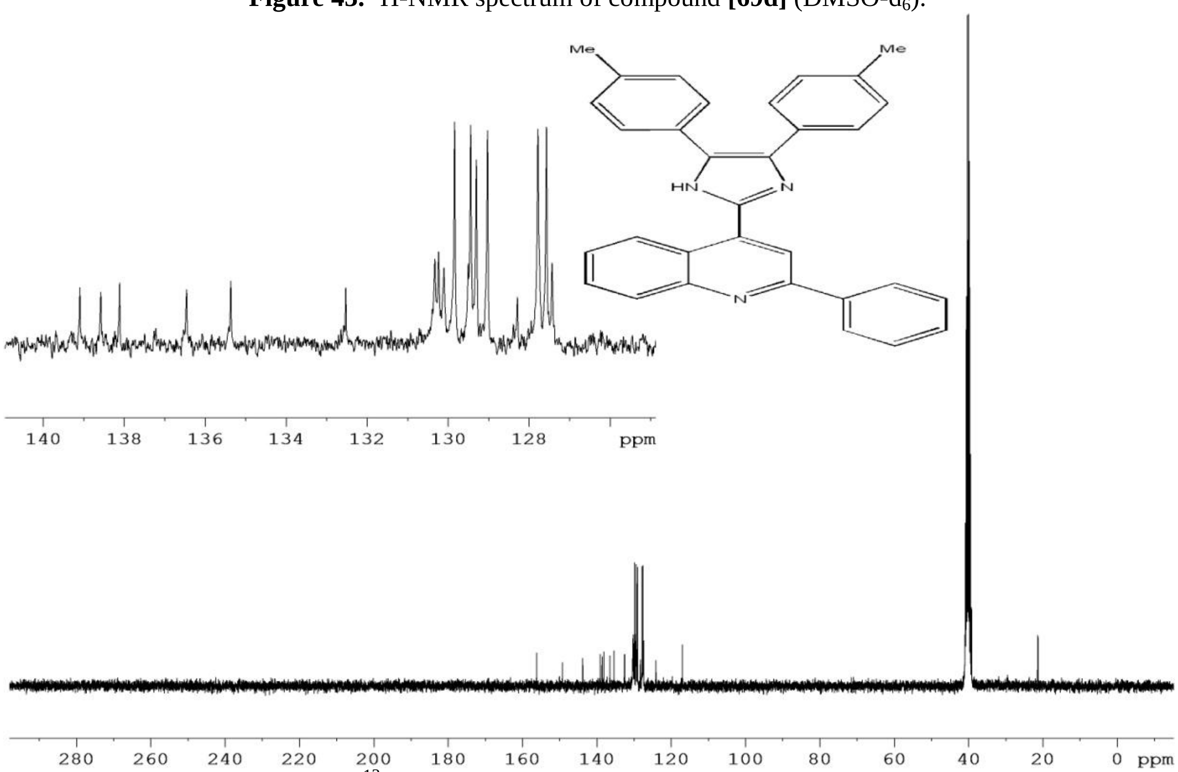


Figure 44. ^{13}C-NMR spectrum of compound **[69d] (DMSO-d_6).**

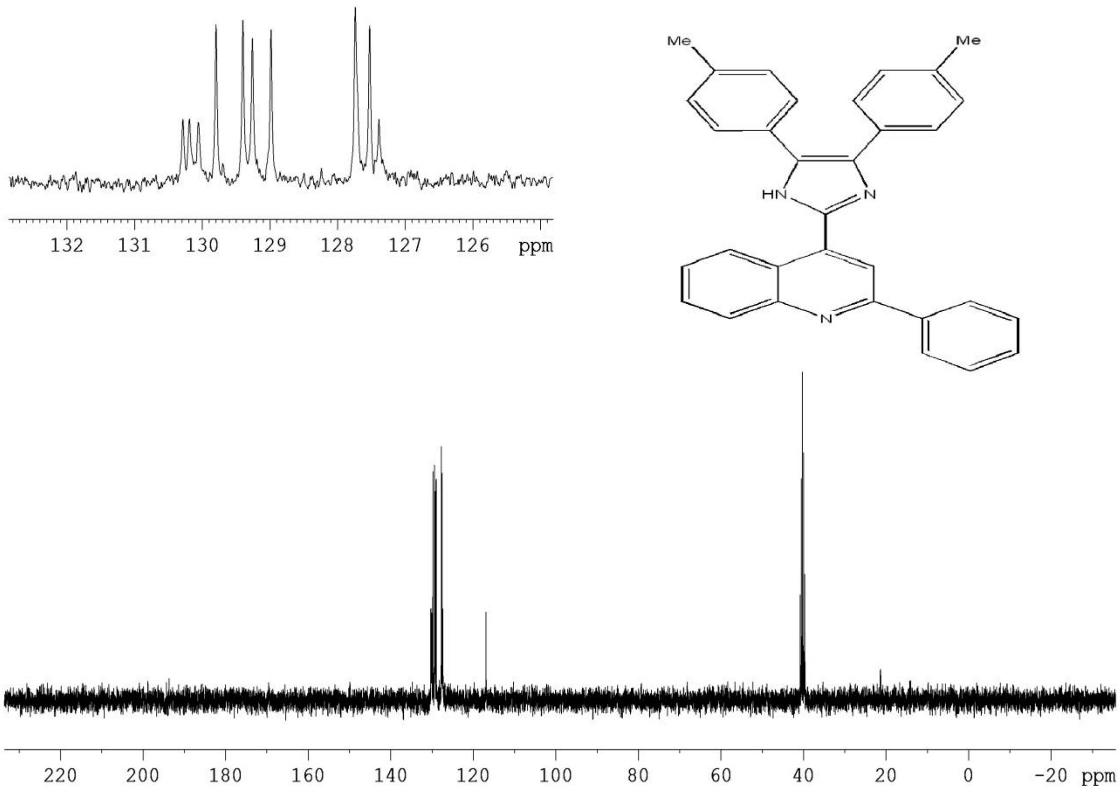


Figure 45. DEPT 135 spectrum of compound [69**d**] (DMSO-d_6).

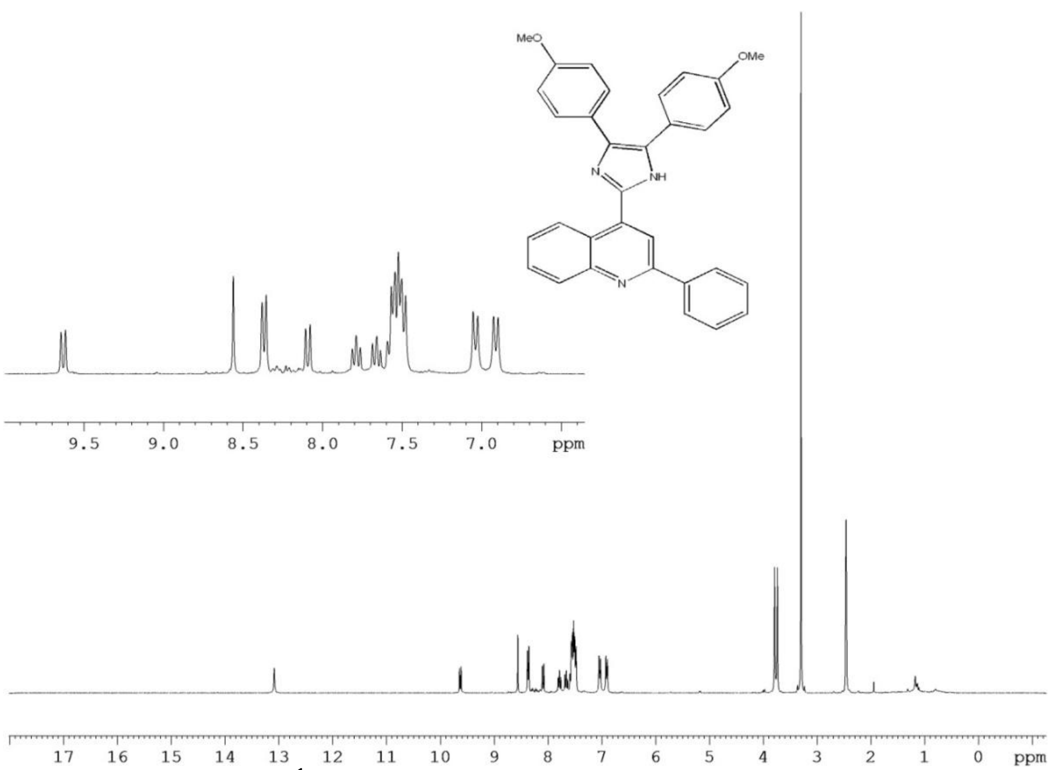


Figure 46. ^{1}H-NMR spectrum of compound [69e] (DMSO-d_6).

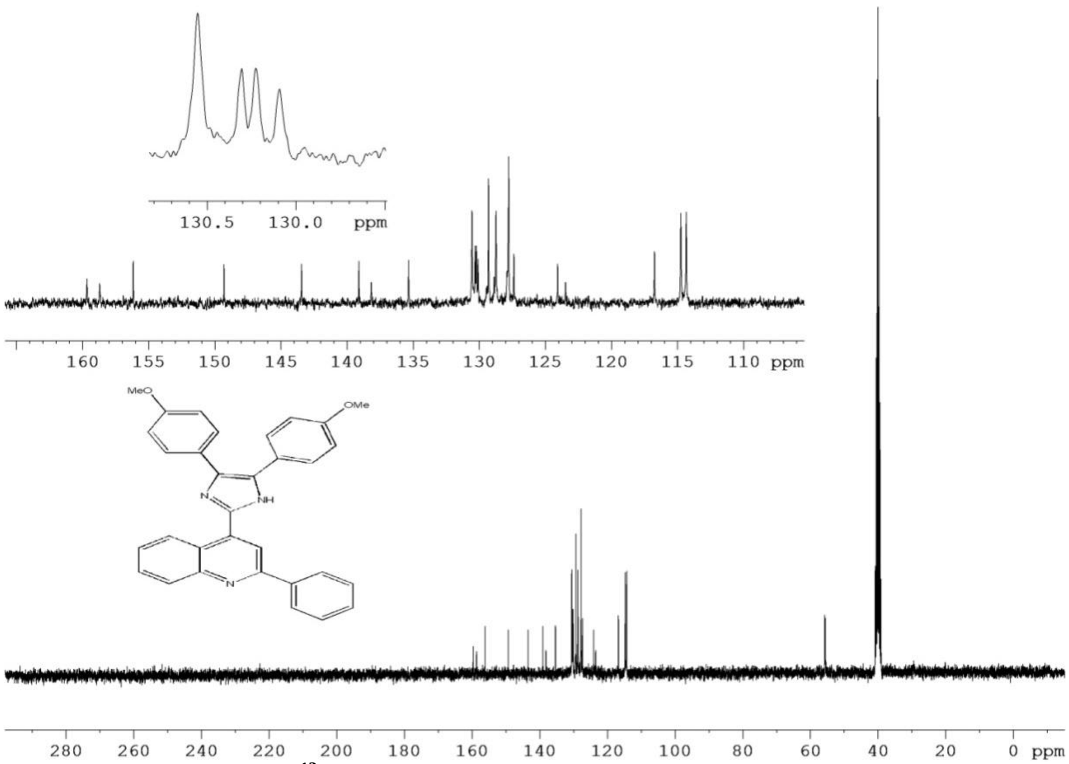


Figure 47. [13] C-NMR spectrum of compound [69e] (DMSO-d$_6$).

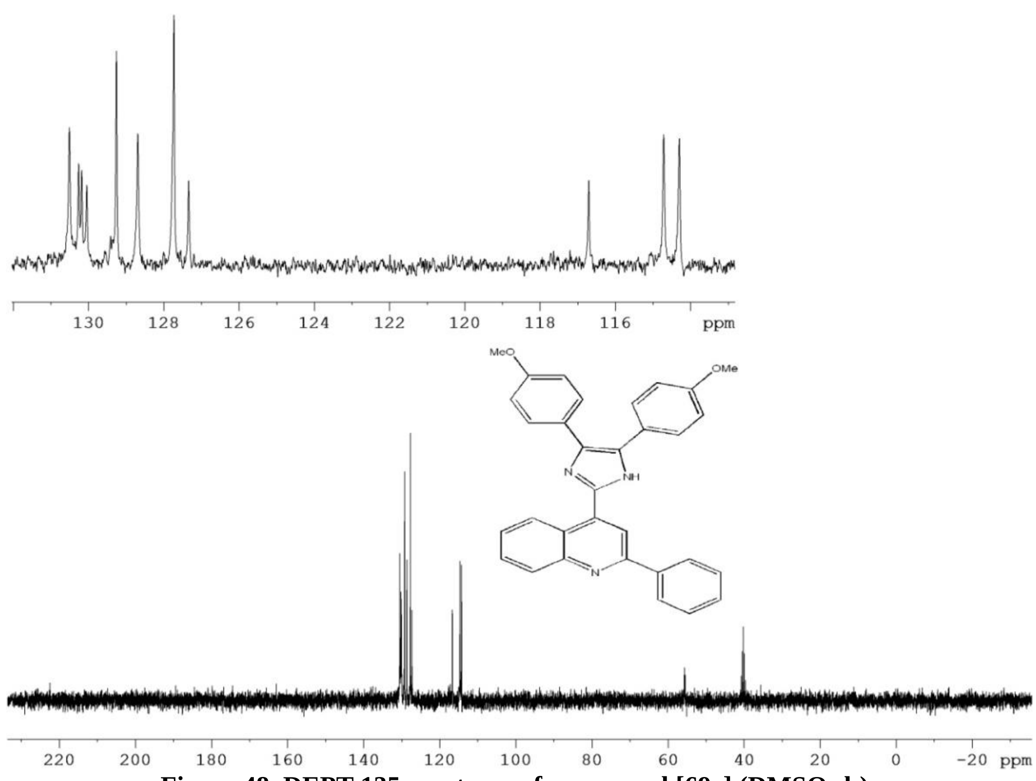


Figure 48. DEPT 135 spectrum of compound [69e] (DMSO-d$_6$).

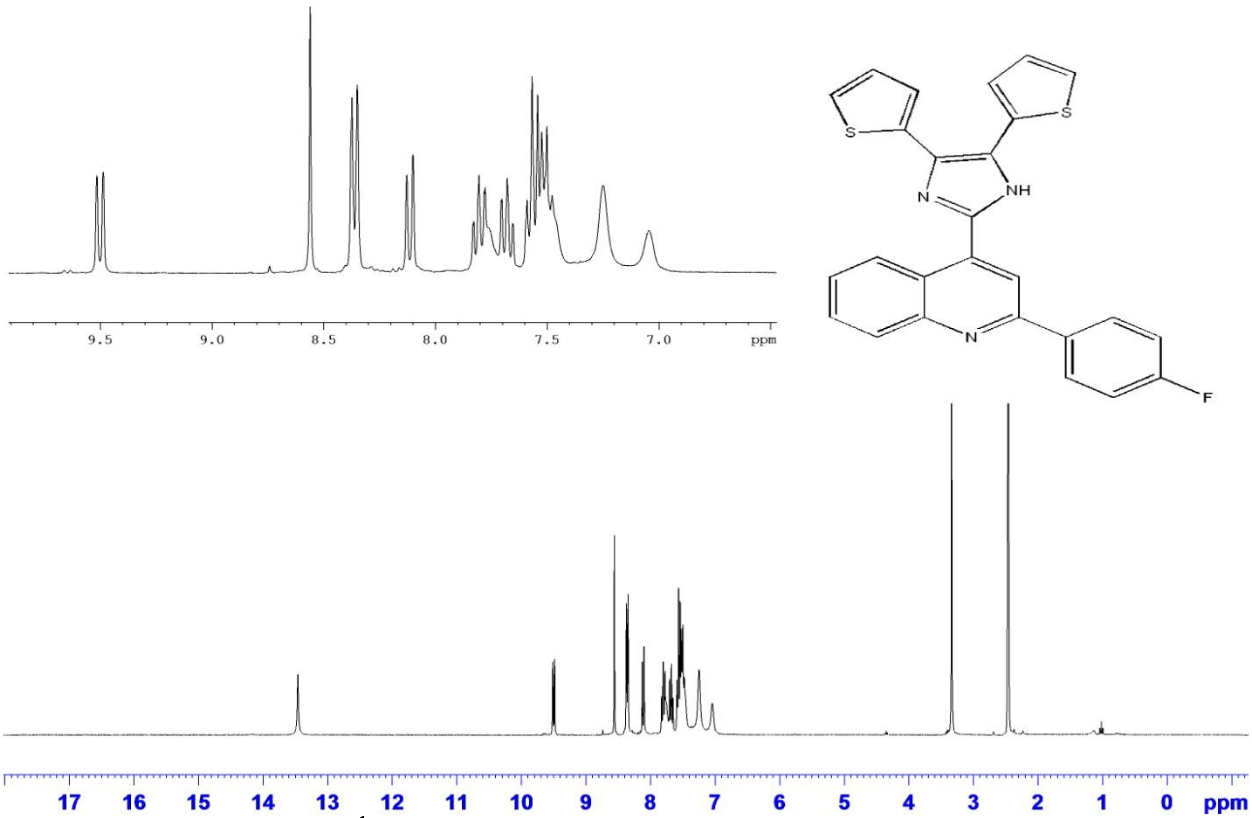


Figure 49. [1]H-NMR spectrum of compound [69h] (DMSO-d_6).

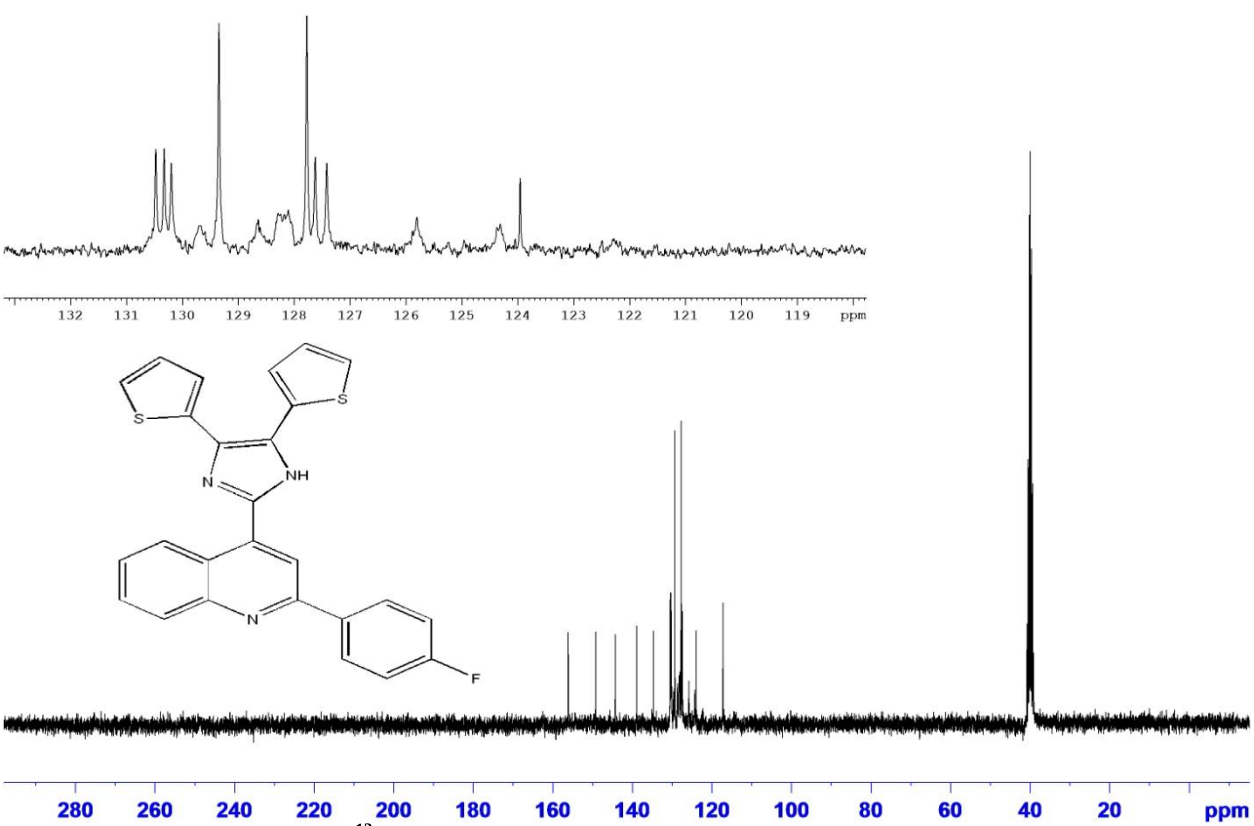


Figure 50. [13]C-NMR spectrum of compound [69h] (DMSO-d_6).

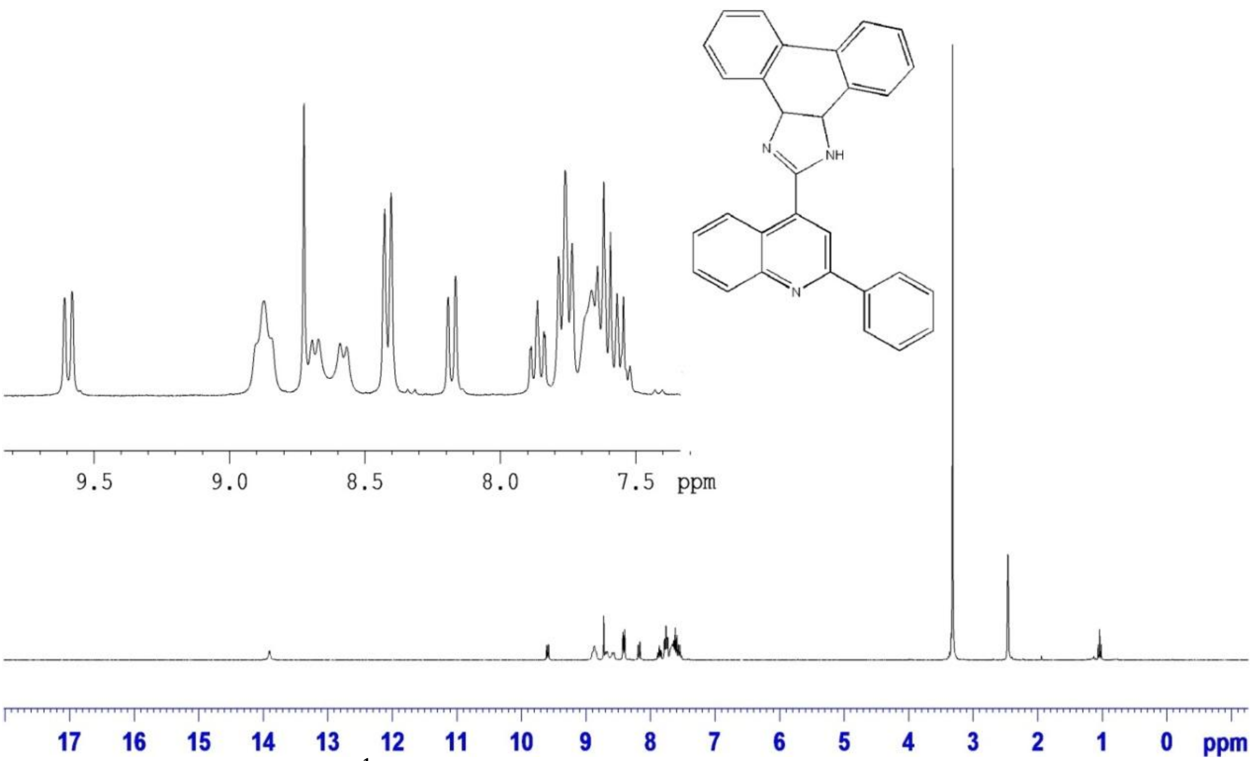


Figure 51. [1]H-NMR spectrum of compound [69i] (DMSO-d_6).

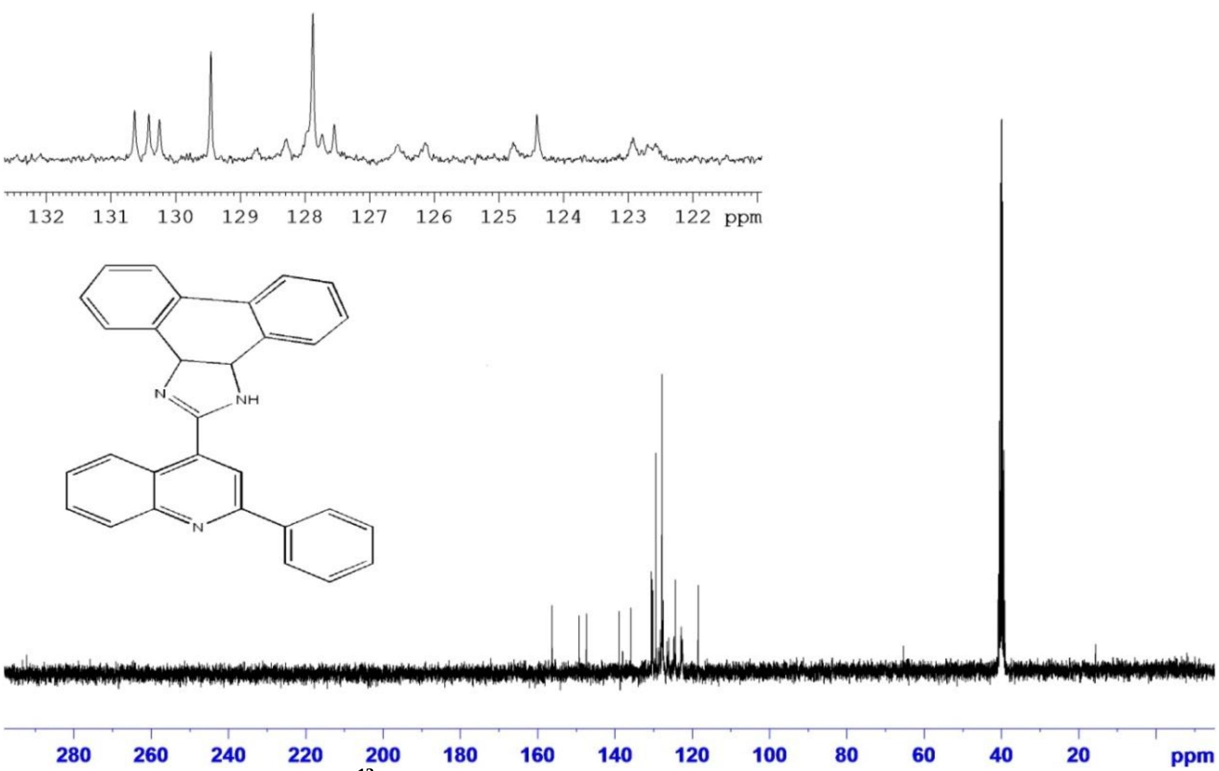


Figure 52. [13] C-NMR spectrum of compound [69i] (DMSO-d_6).

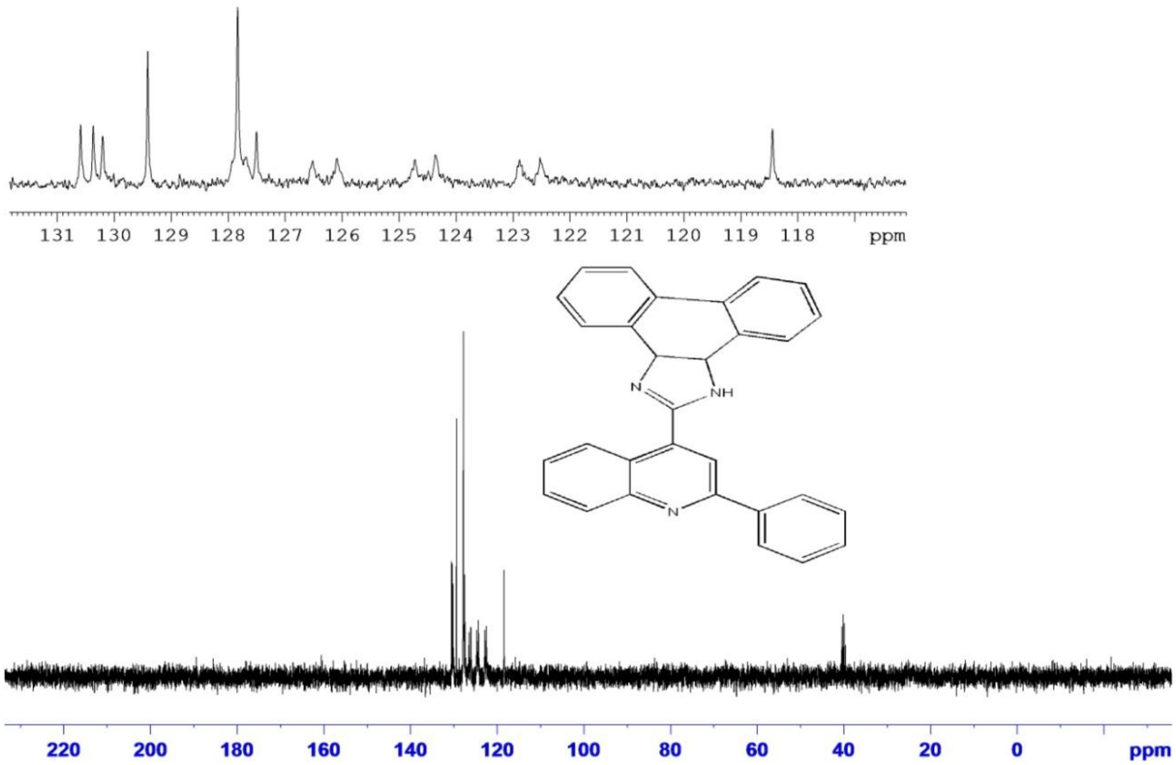


Figure 53. DEPT 135 spectrum of compound [69i] (DMSO-d_6).

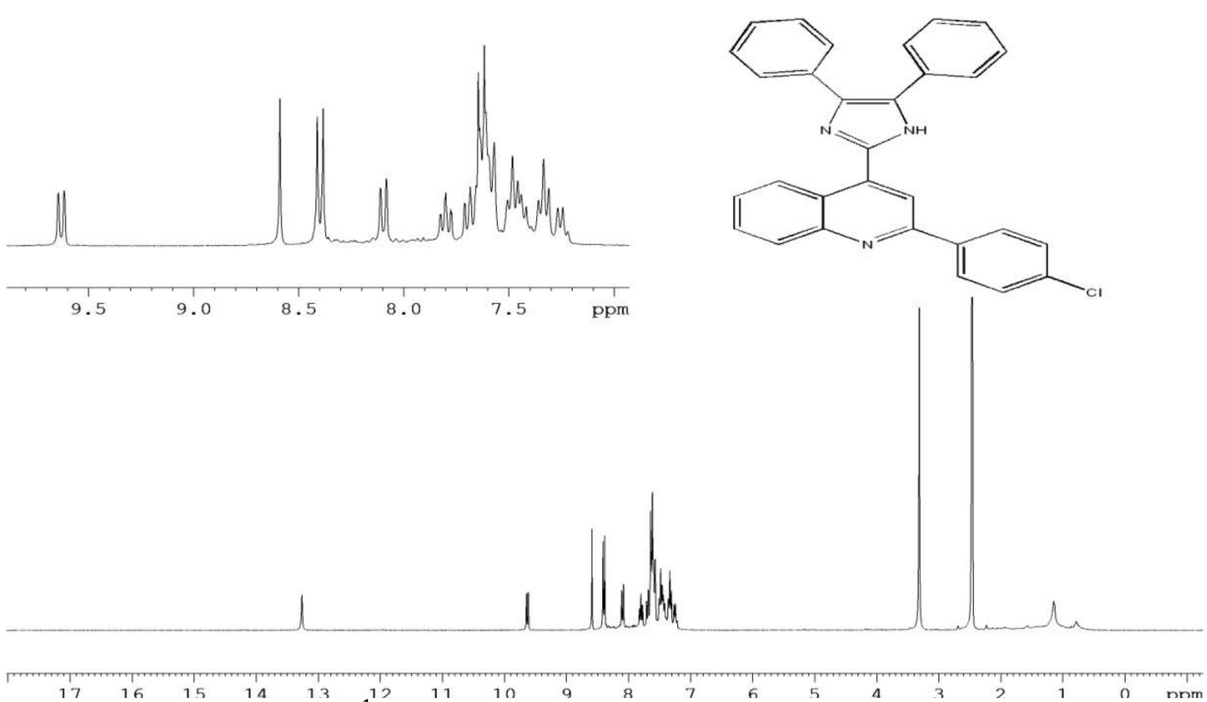


Figure 54. ^{1}H-NMR spectrum of compound [70a] (DMSO-d_6).

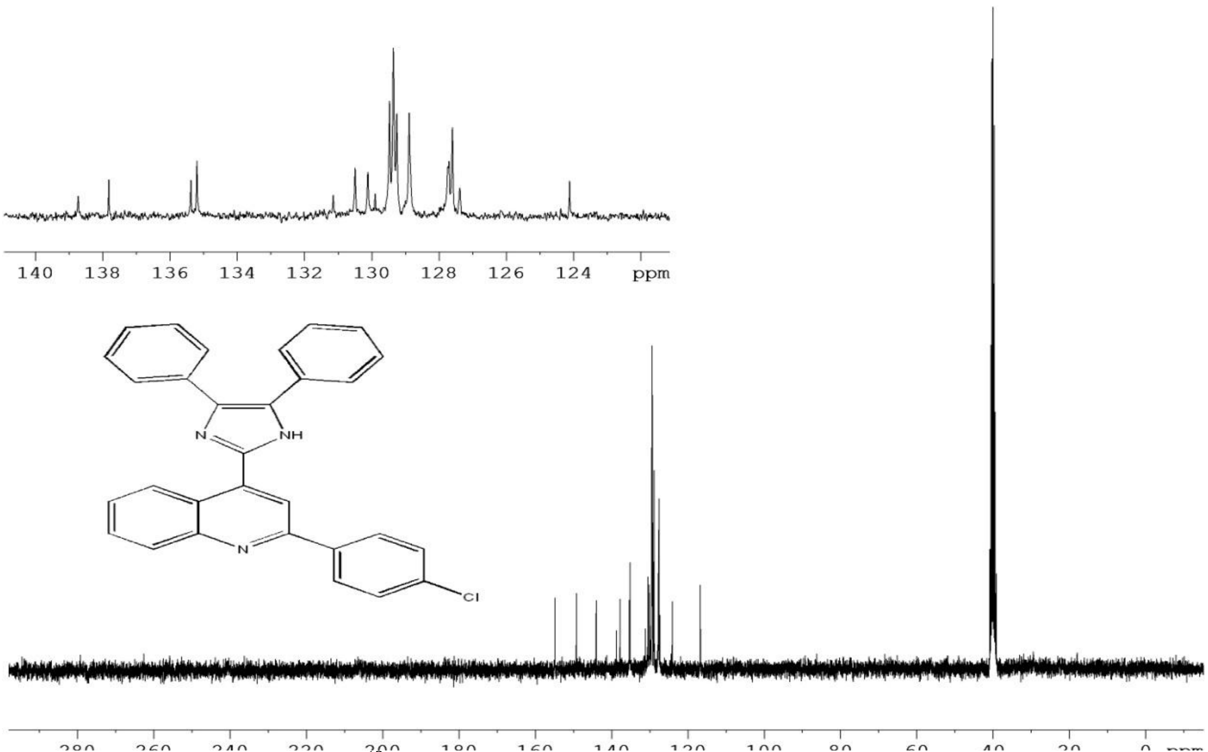


Figure 55. ^{13}C-NMR spectrum of compound [**70a**] (DMSO-d_6).

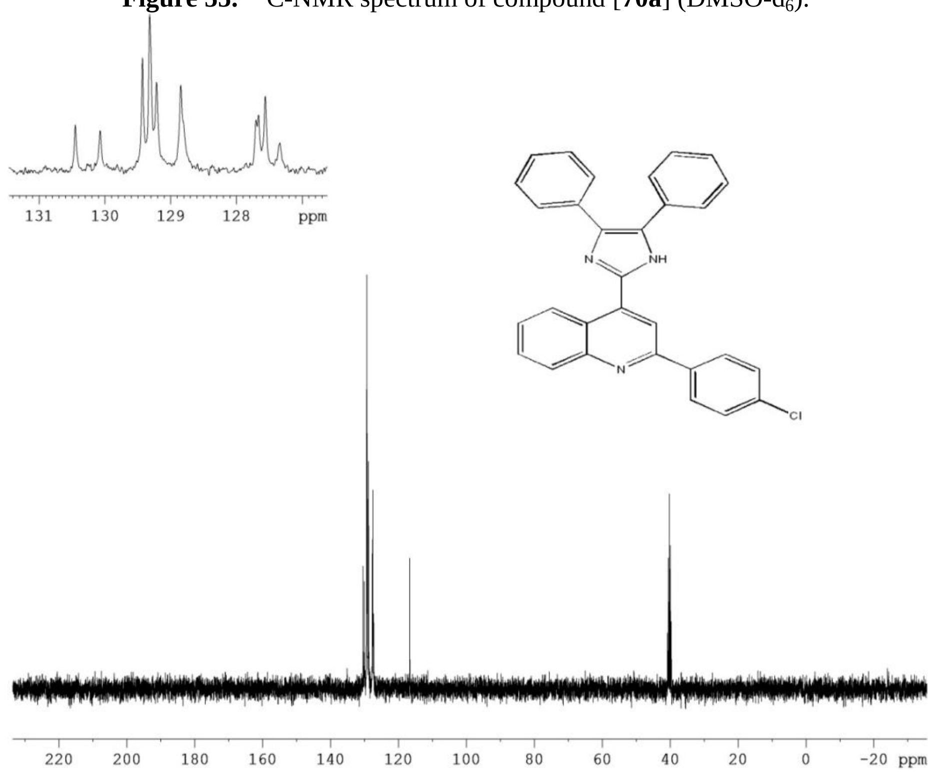


Figure 56. DEPT 135 spectrum of compound [**70a**] (DMSO-d_6).

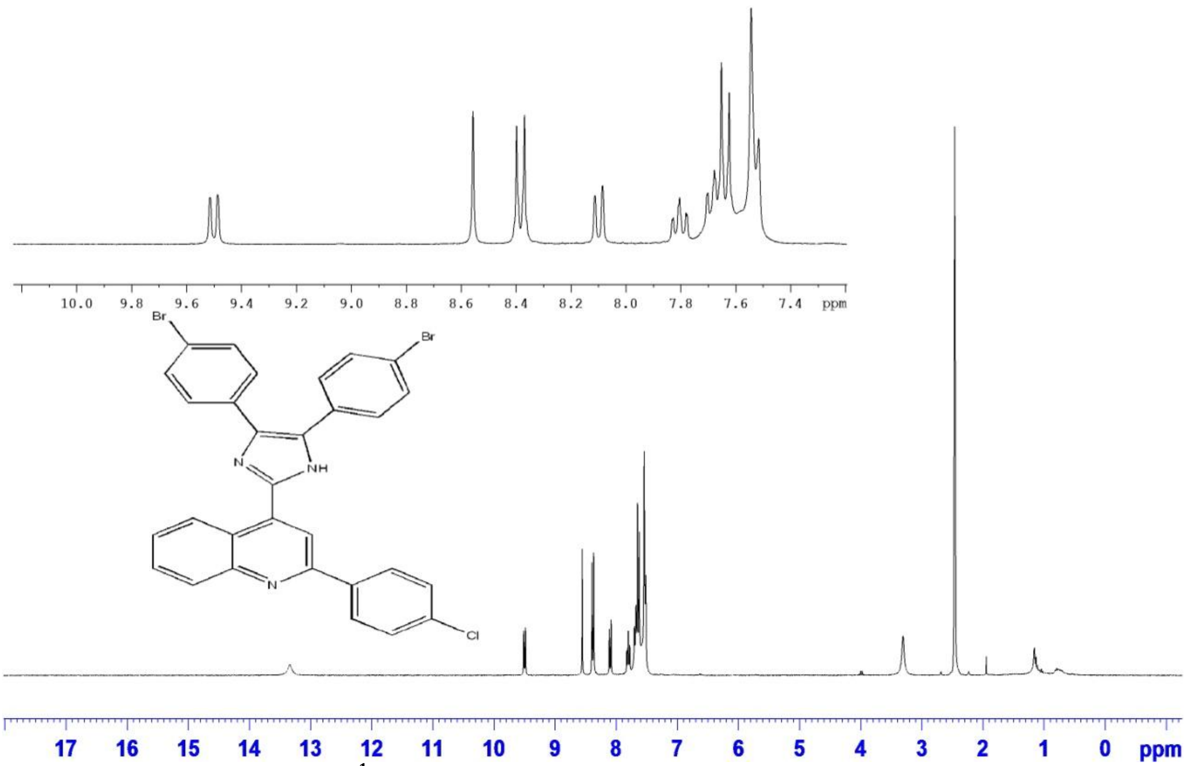


Figure 57. ^{1}H-NMR spectrum of compound [70b] (DMSO-d_6).

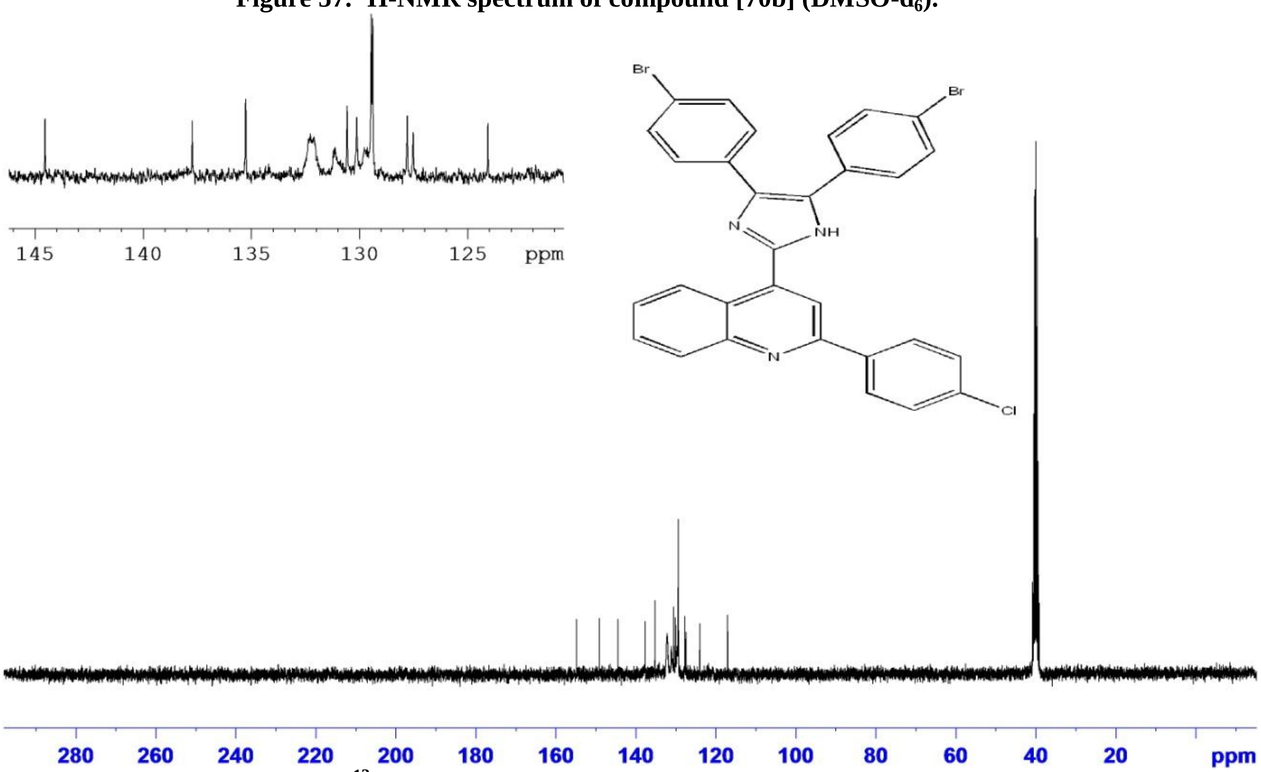


Figure 58. ^{13}C-NMR spectrum of compound [70b] (DMSO-d_6).

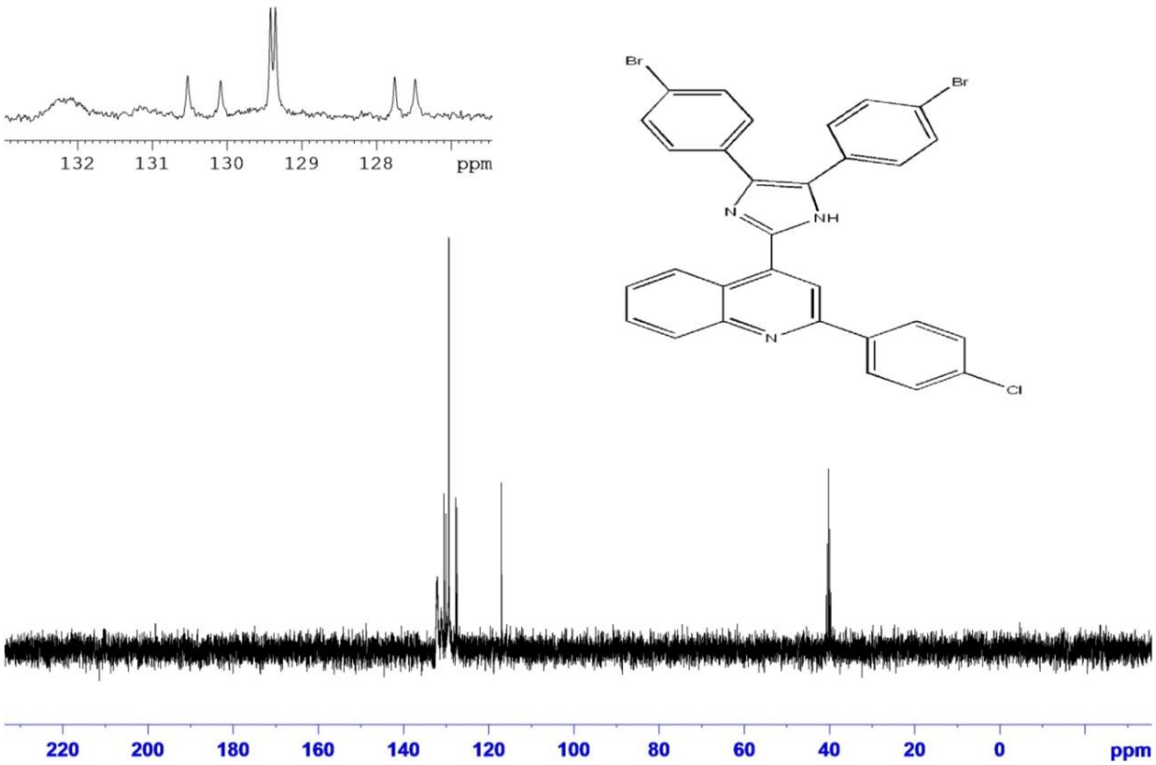


Figure 59. DEPT 135 spectrum of compound [70b] (DMSO-d_6).

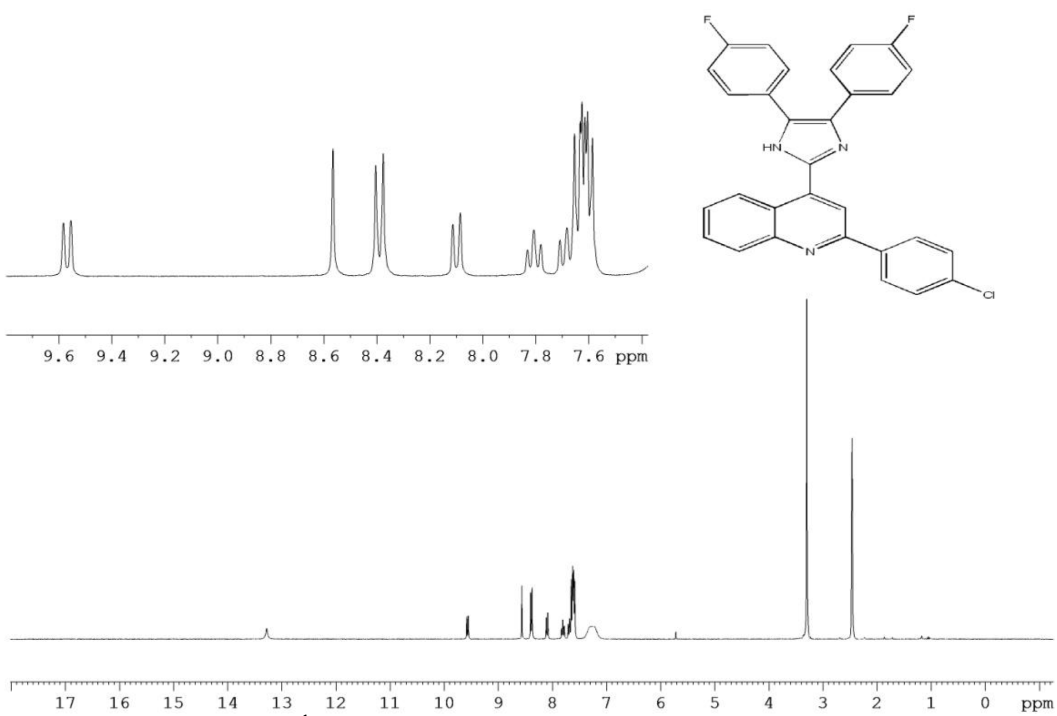


Figure 60. ^{1}H-NMR spectrum of compound [70c] (DMSO-d_6).

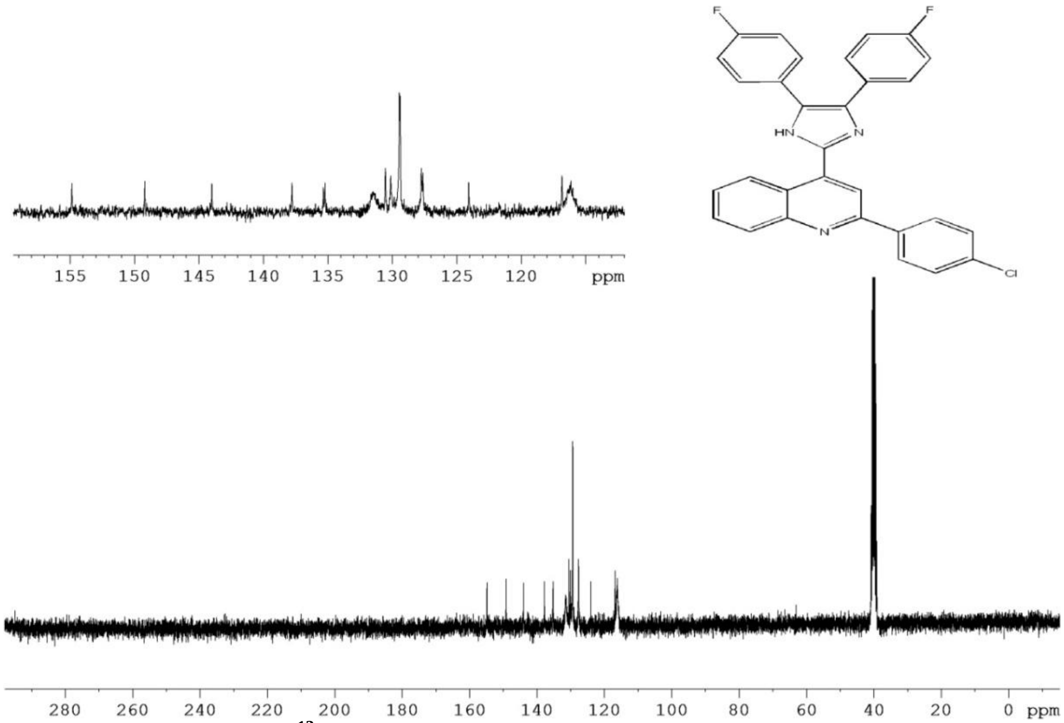


Figure 61. ^{13}C-NMR spectrum of compound [70c] (DMSO-d_6).

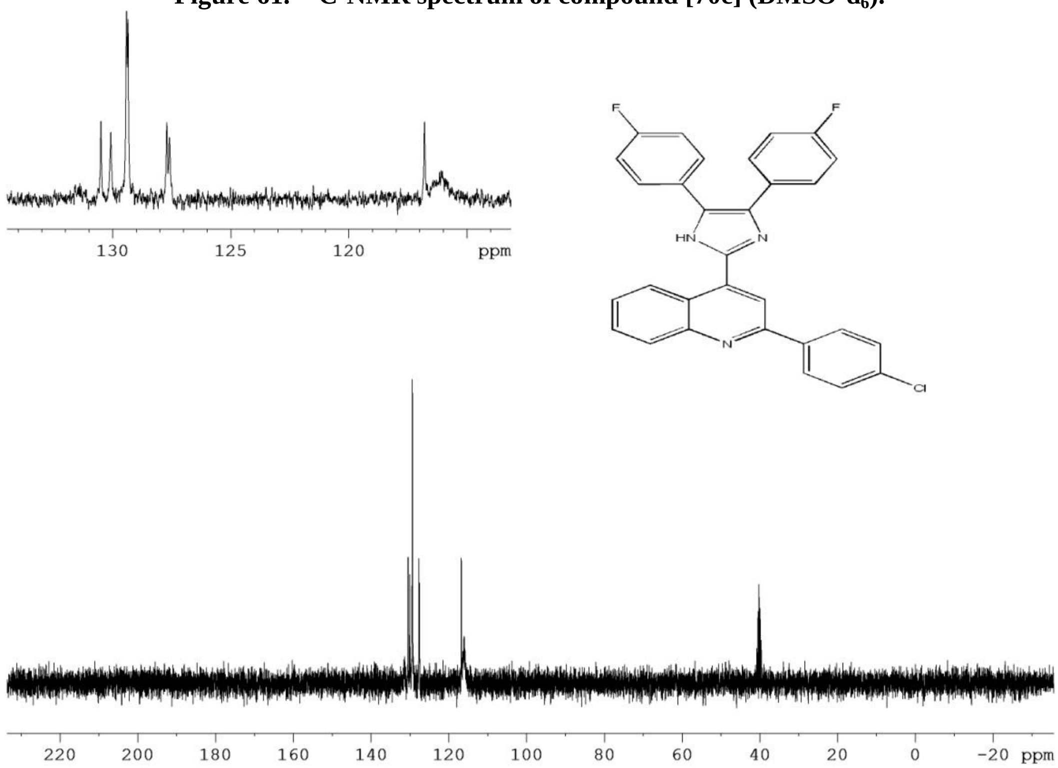


Figure 62. DEPT 135 spectrum of compound [70c] (DMSO-d_6).

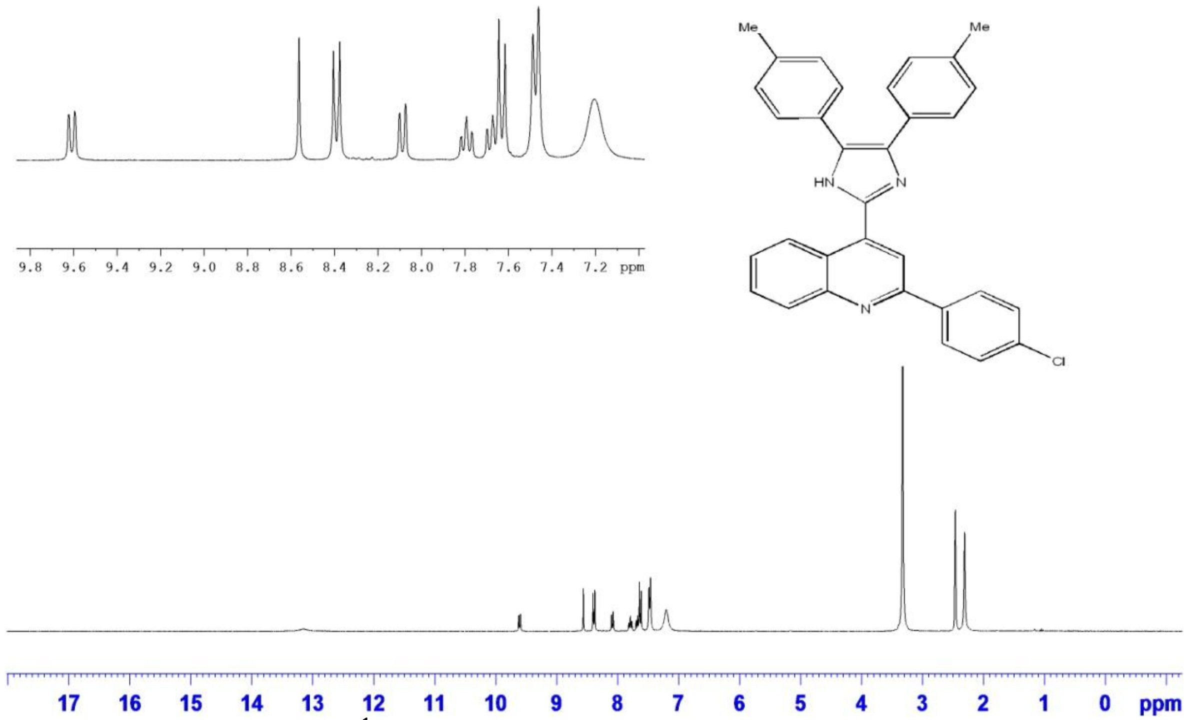


Figure 63. [1]H-NMR spectrum of compound [70d] (DMSO-d_6).

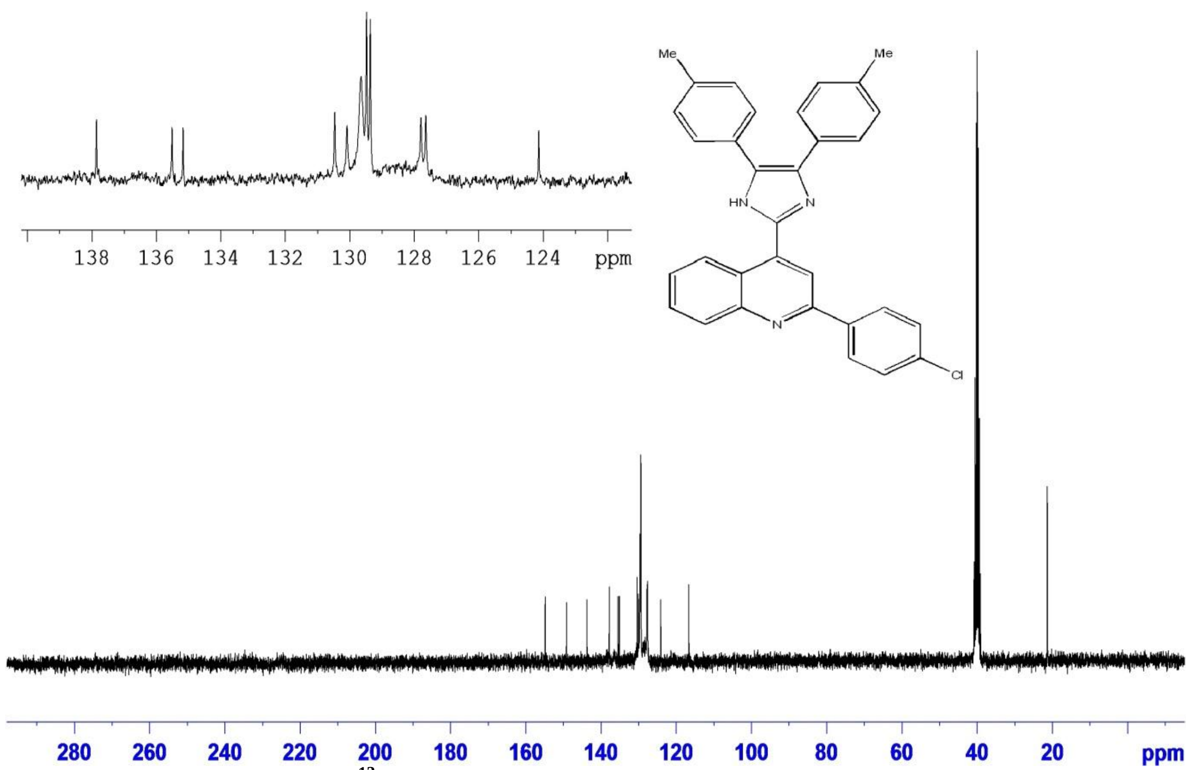


Figure 64. [13]C-NMR spectrum of compound [70d] (DMSO-d_6).

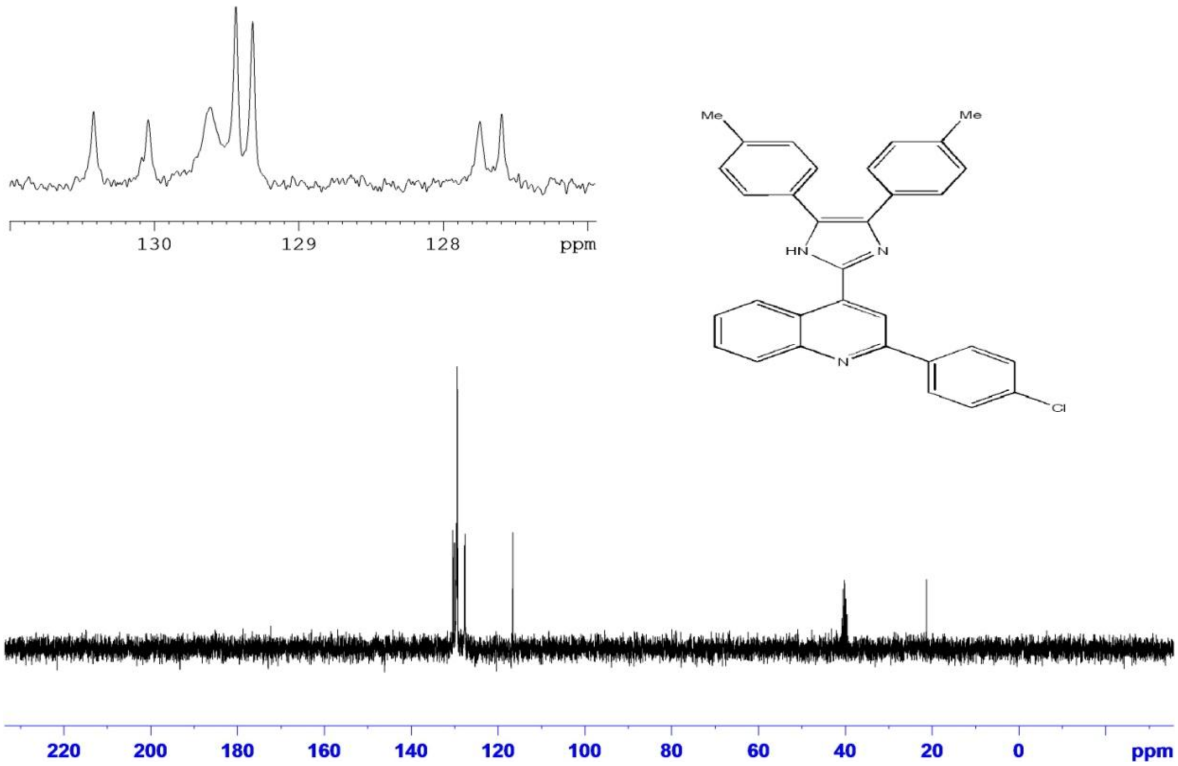


Figure 65. DEPT 135 spectrum of compound [70d] (DMSO-d_6).

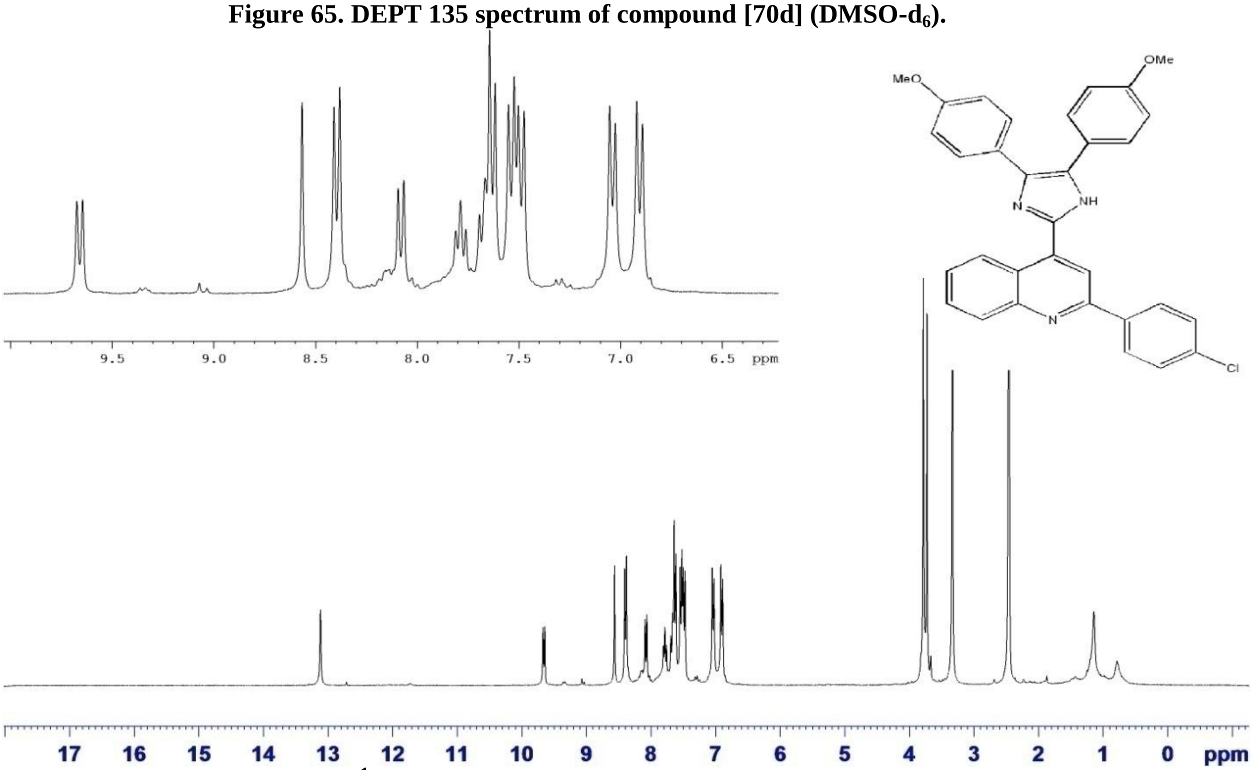


Figure 66. ^{1}H-NMR spectrum of compound [70e] (DMSO-d_6).

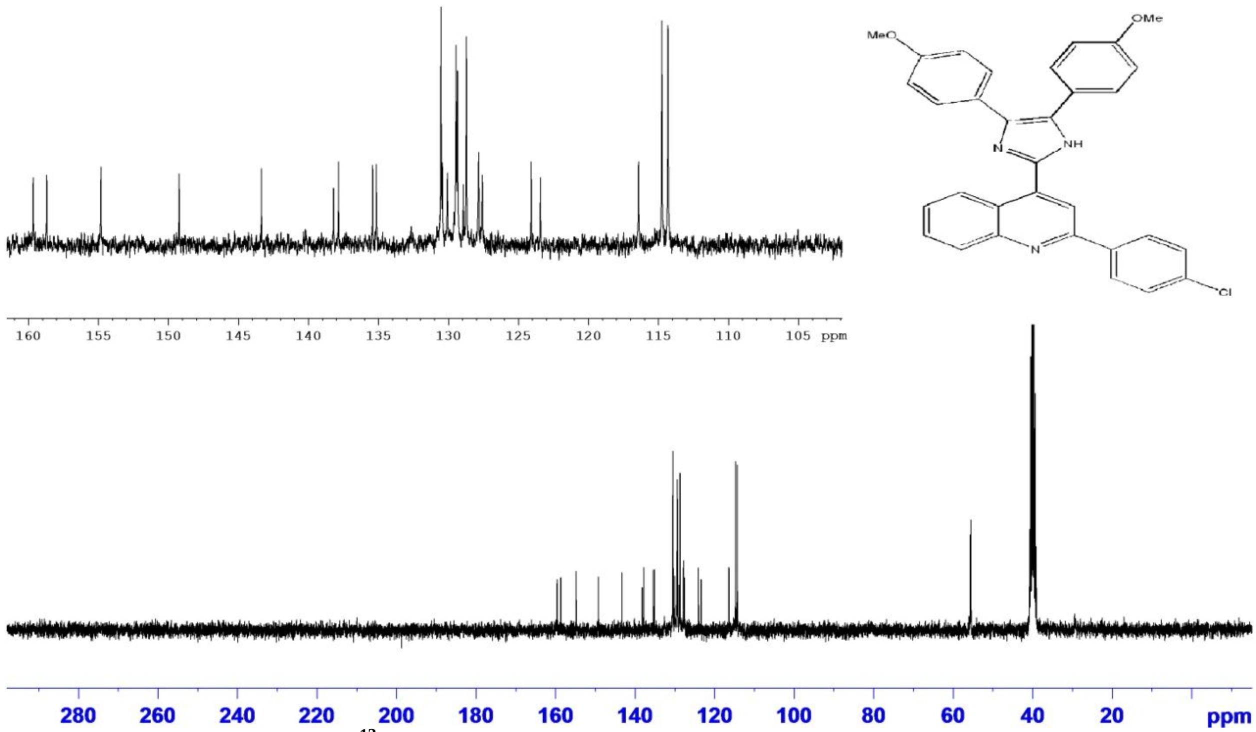


Figure 67. ^{13}C-NMR spectrum of compound [70e] (DMSO-d_6).

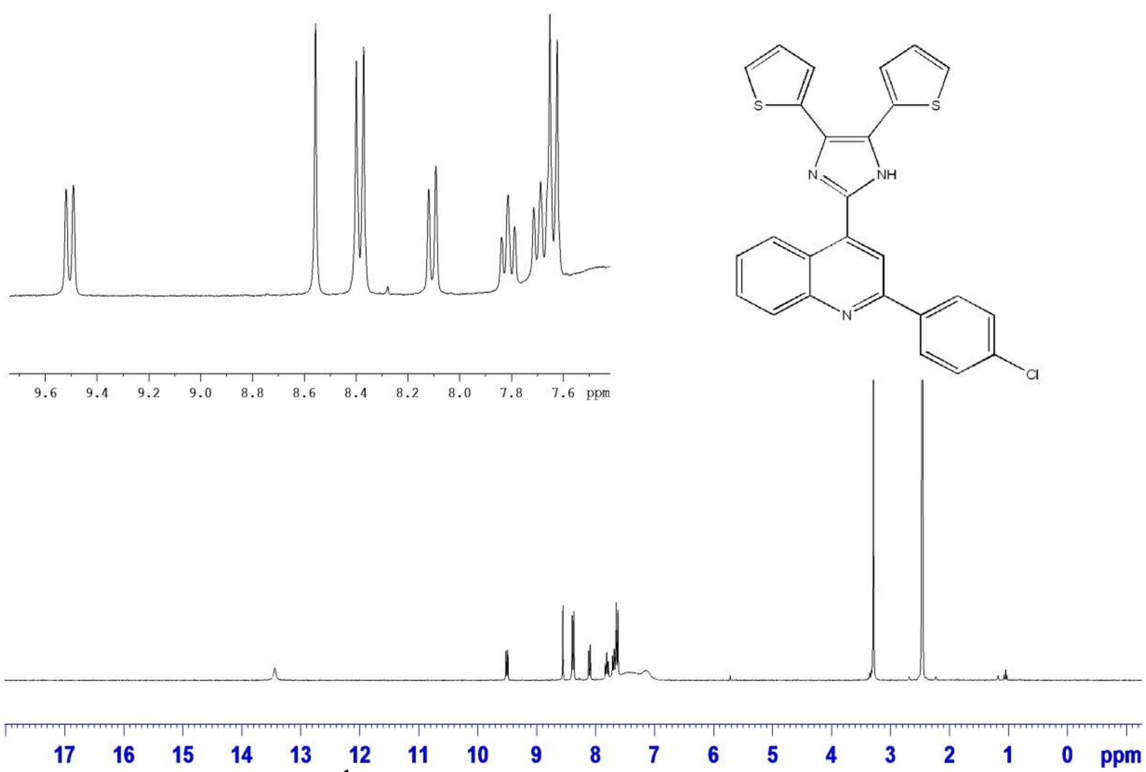


Figure 68. ^{1}H-NMR spectrum of compound [70h] (DMSO-d_6).

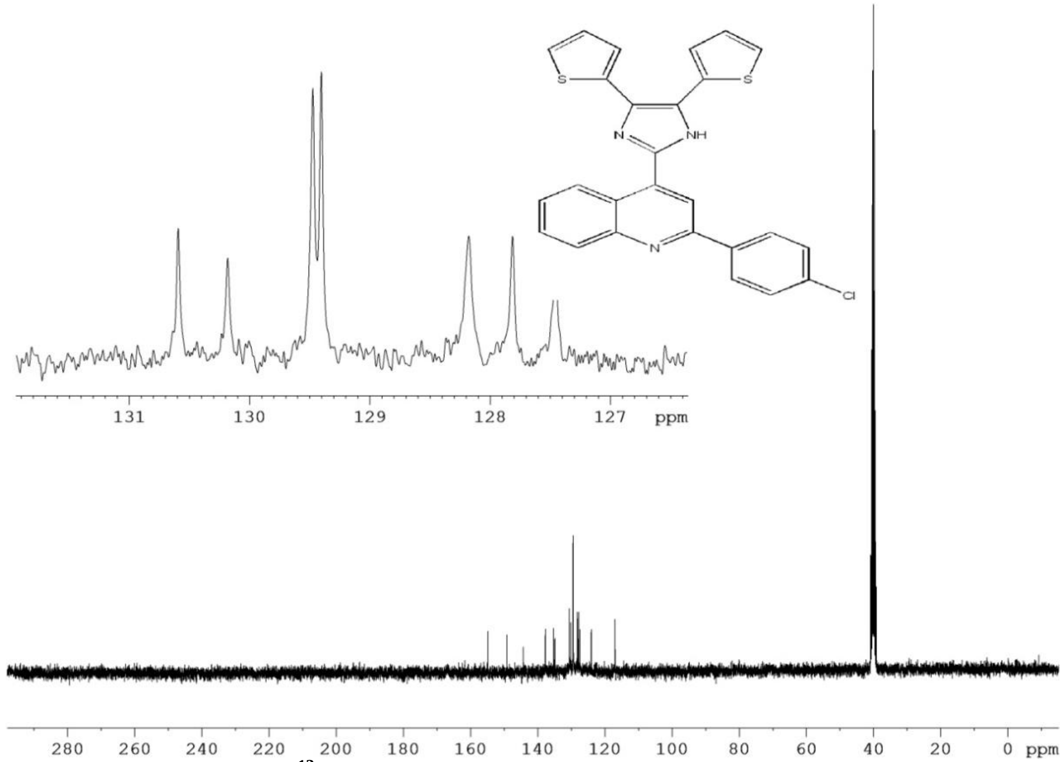


Figure 69. ^{13}C-NMR spectrum of compound [70h] (DMSO-d_6).

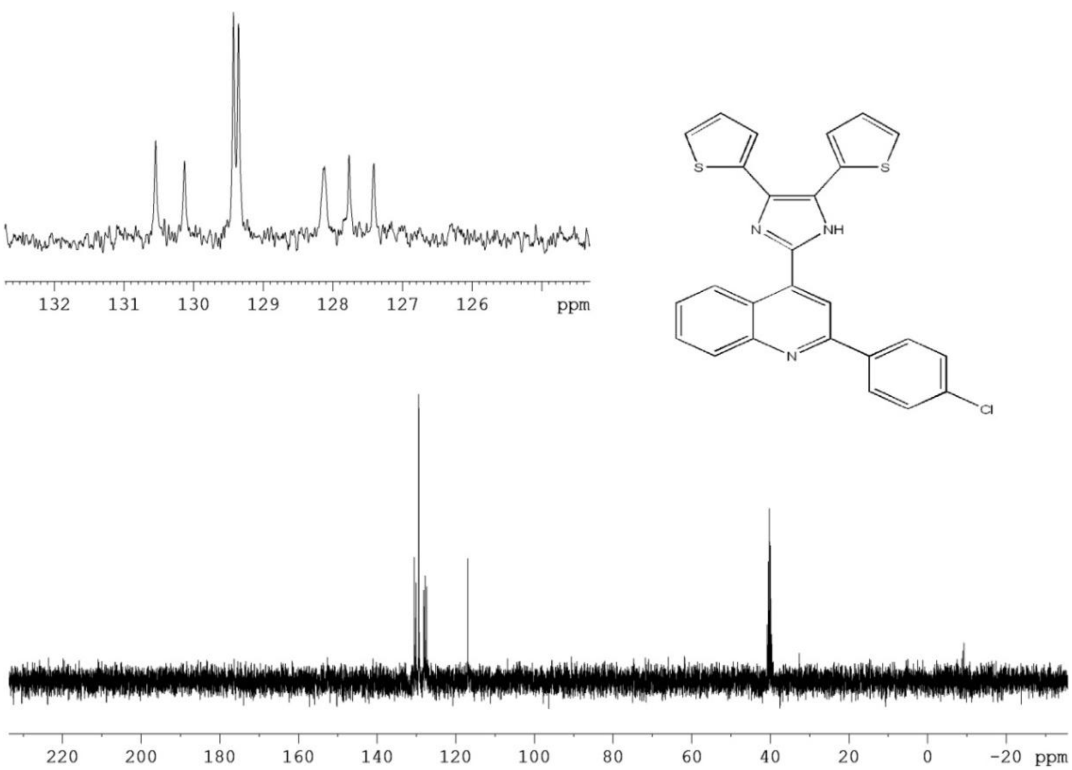


Figure 70. DEPT 135 spectrum of compound [70h] (DMSO-d_6).

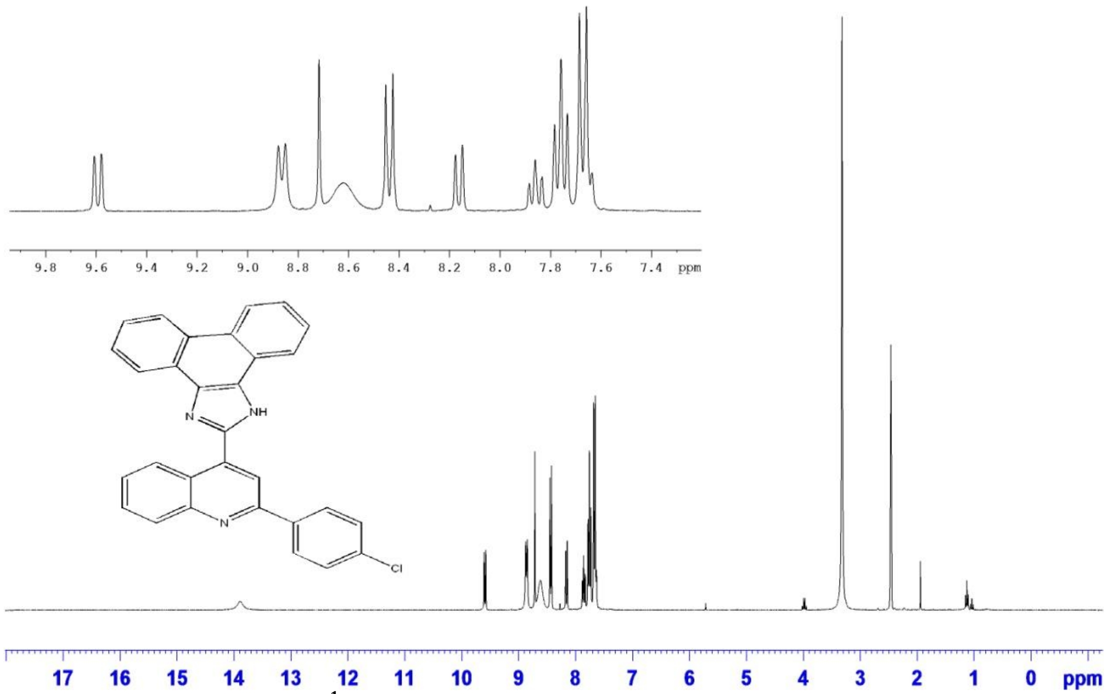


Figure 71. ^{1}H-NMR spectrum of compound [70i] (DMSO-d_6).

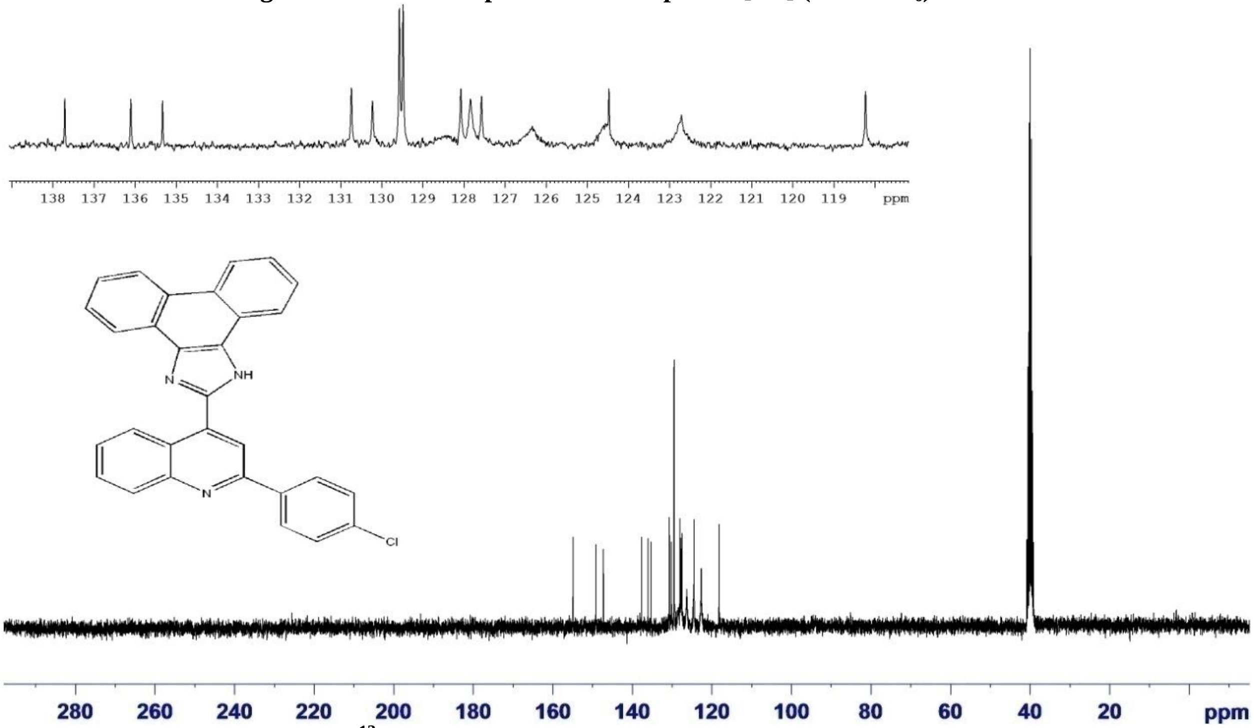


Figure 72. ^{13}C-NMR spectrum of compound [70i] (DMSO-d_6).

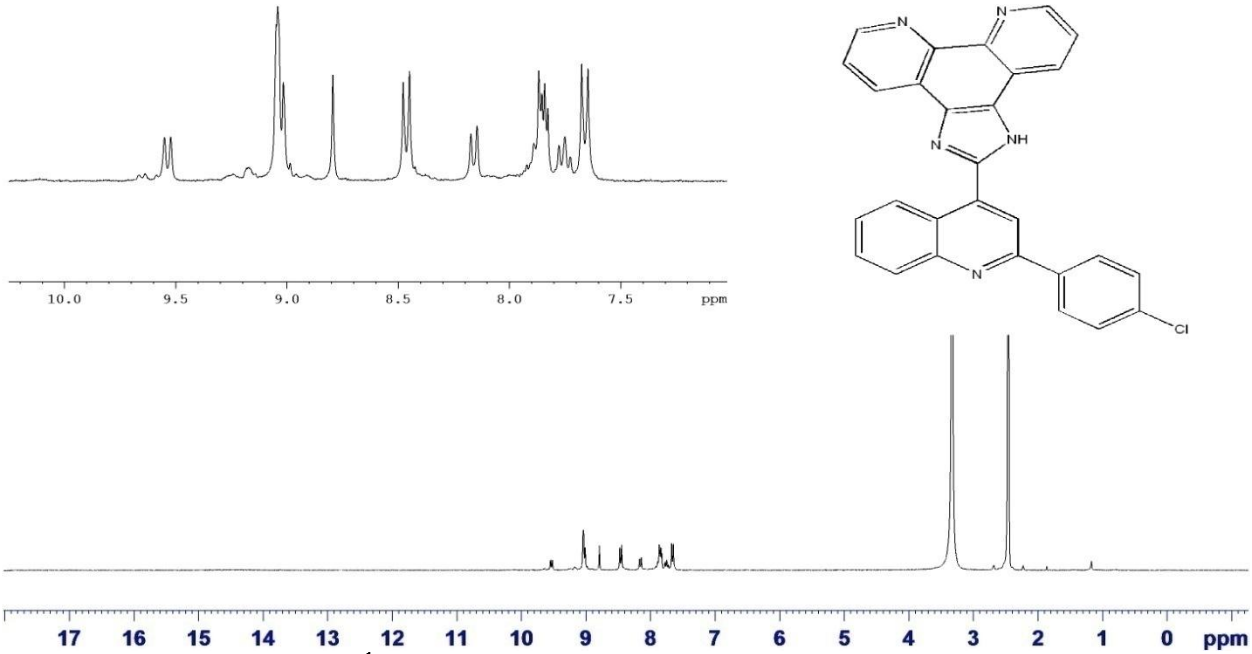


Figure 73. ^{1}H-NMR spectrum of compound [70j] (DMSO-d_6).

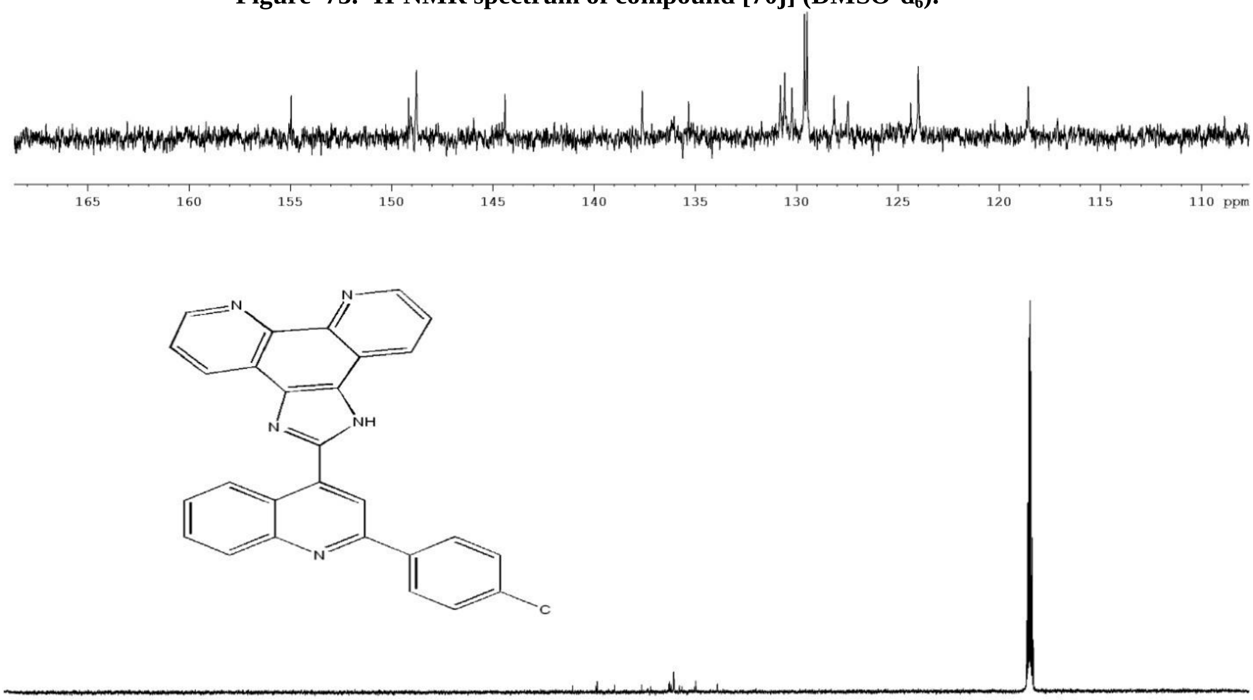


Figure 74. ^{13}C-NMR spectrum of compound [70j] (DMSO-d_6).

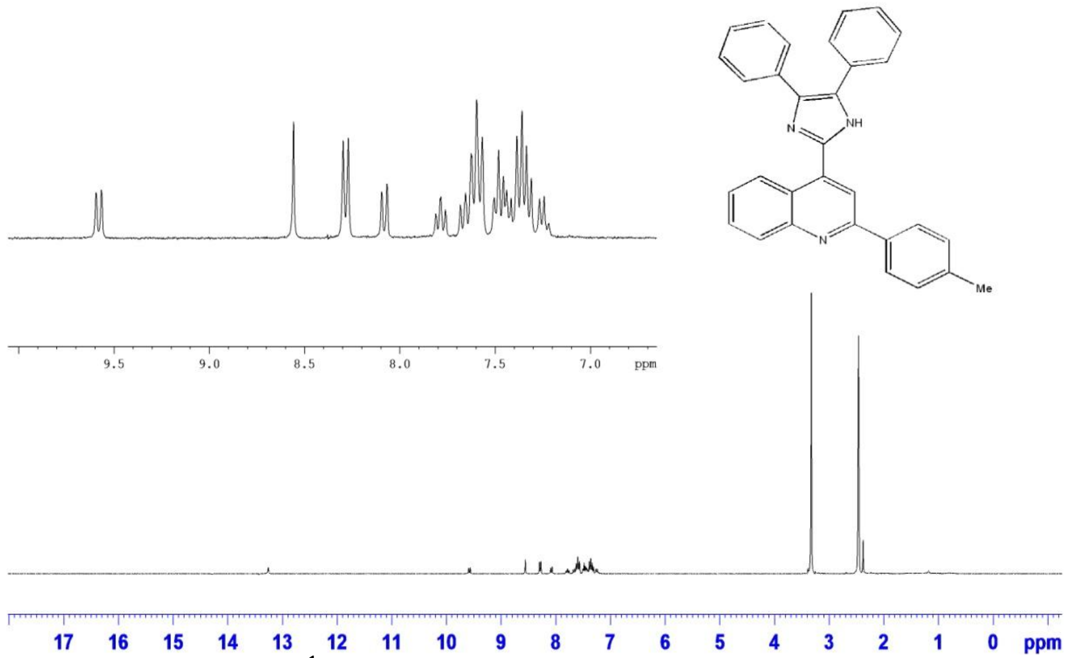


Figure 75. ^{1}H-NMR spectrum of compound [71a] (DMSO-d_6).

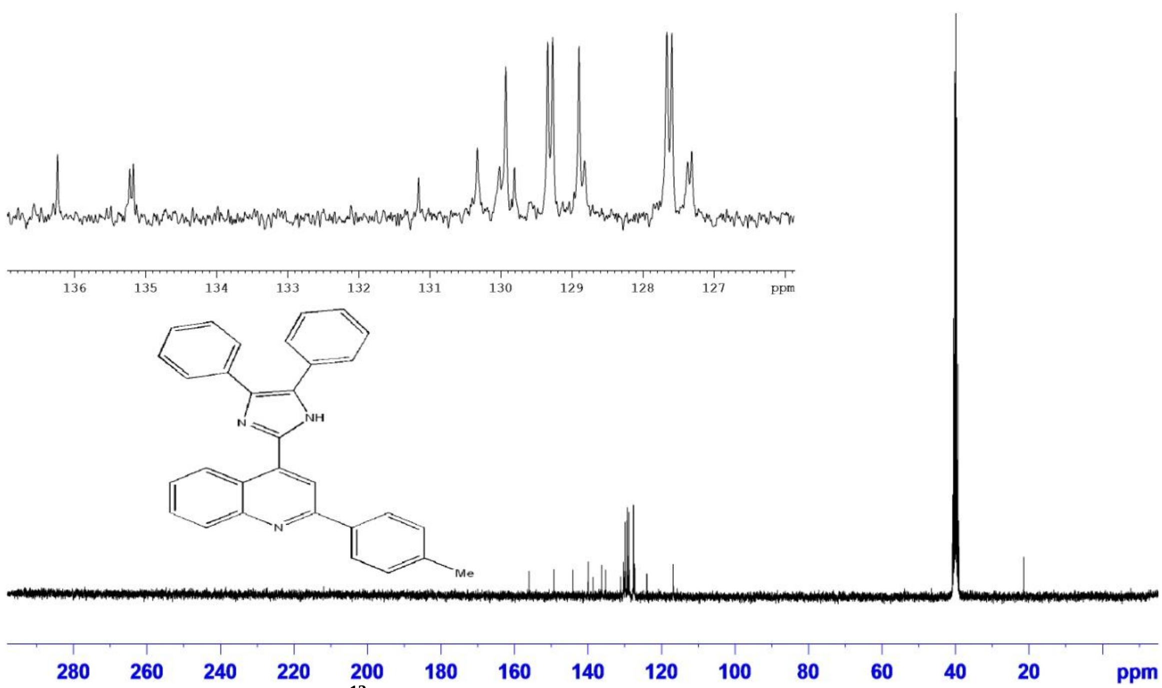


Figure 76. ^{13}C-NMR spectrum of compound [71a] (DMSO-d_6).

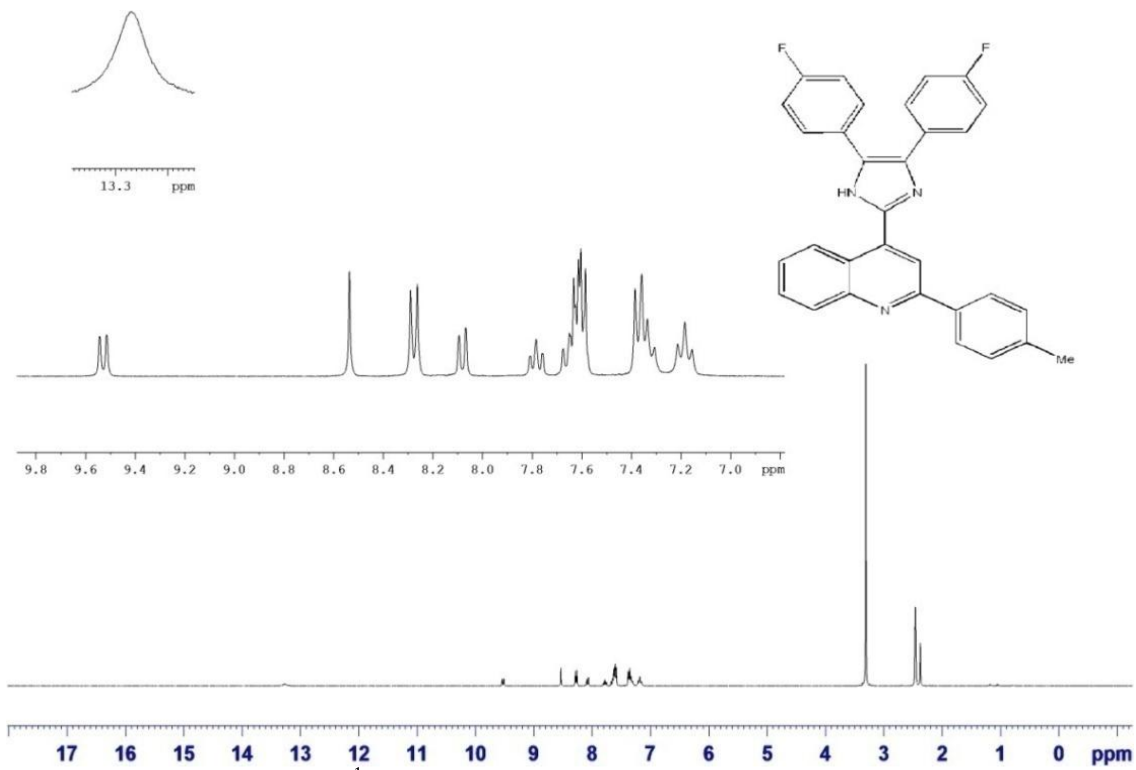


Figure 77. ^{1}H-NMR spectrum of compound **[71c]** (DMSO-d_6).

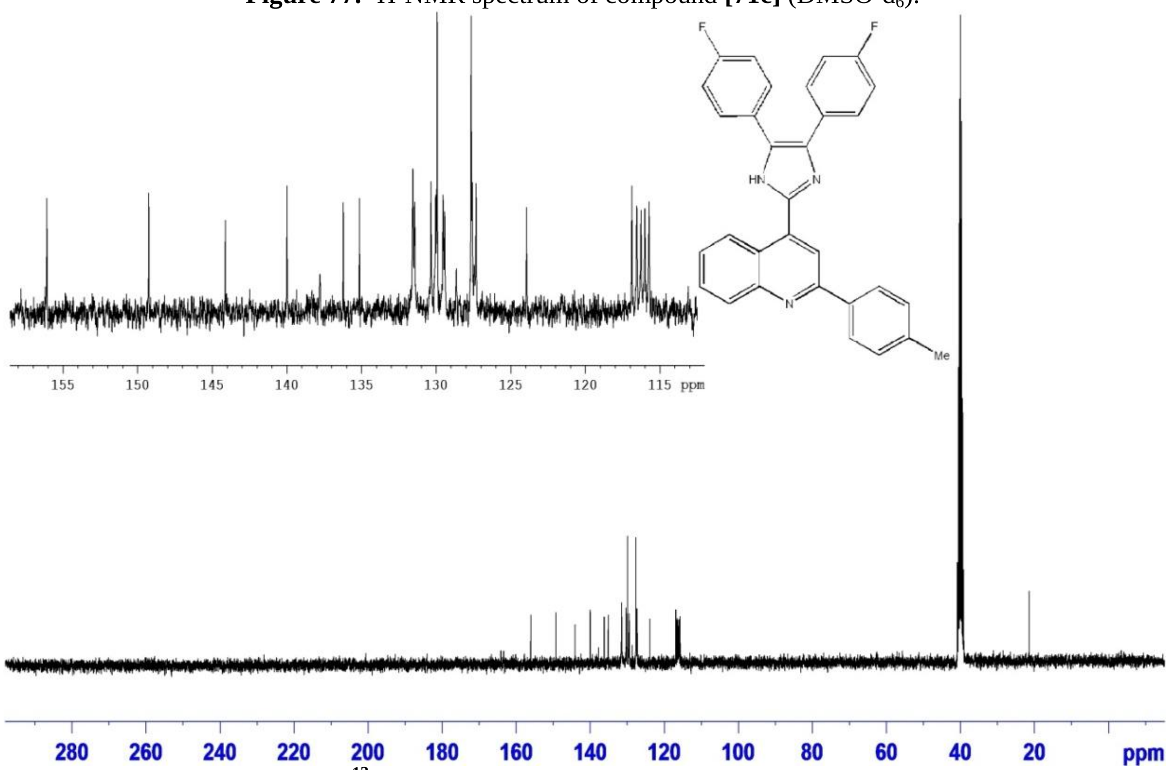


Figure 78. ^{13}C-NMR spectrum of compound [71c] (DMSO-d_6).

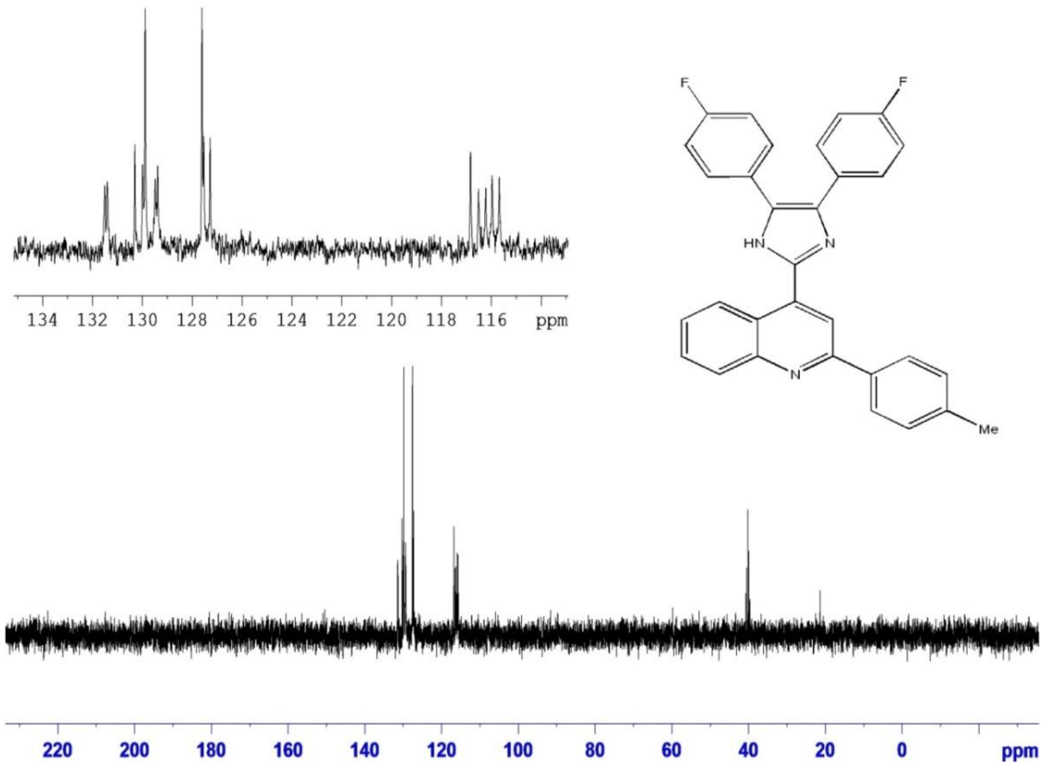


Figure 79. DEPT 135 spectrum of compound [71c] (DMSO-d_6).

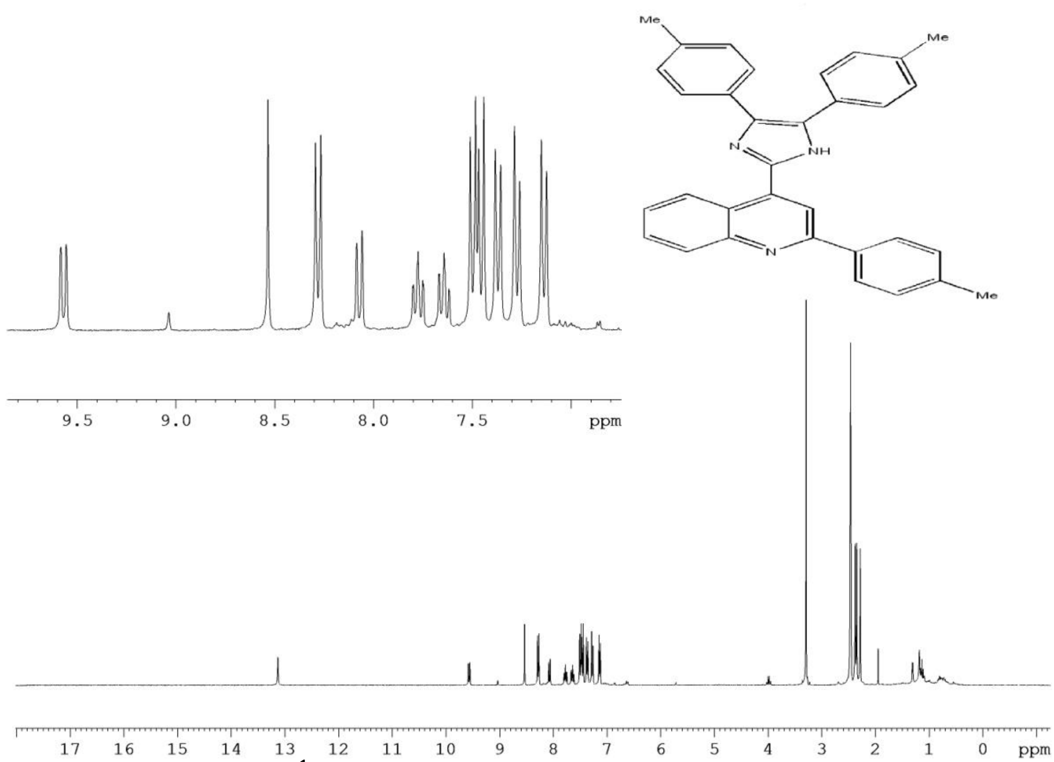


Figure 80. ^{1}H-NMR spectrum of compound [71d] (DMSO-d_6).

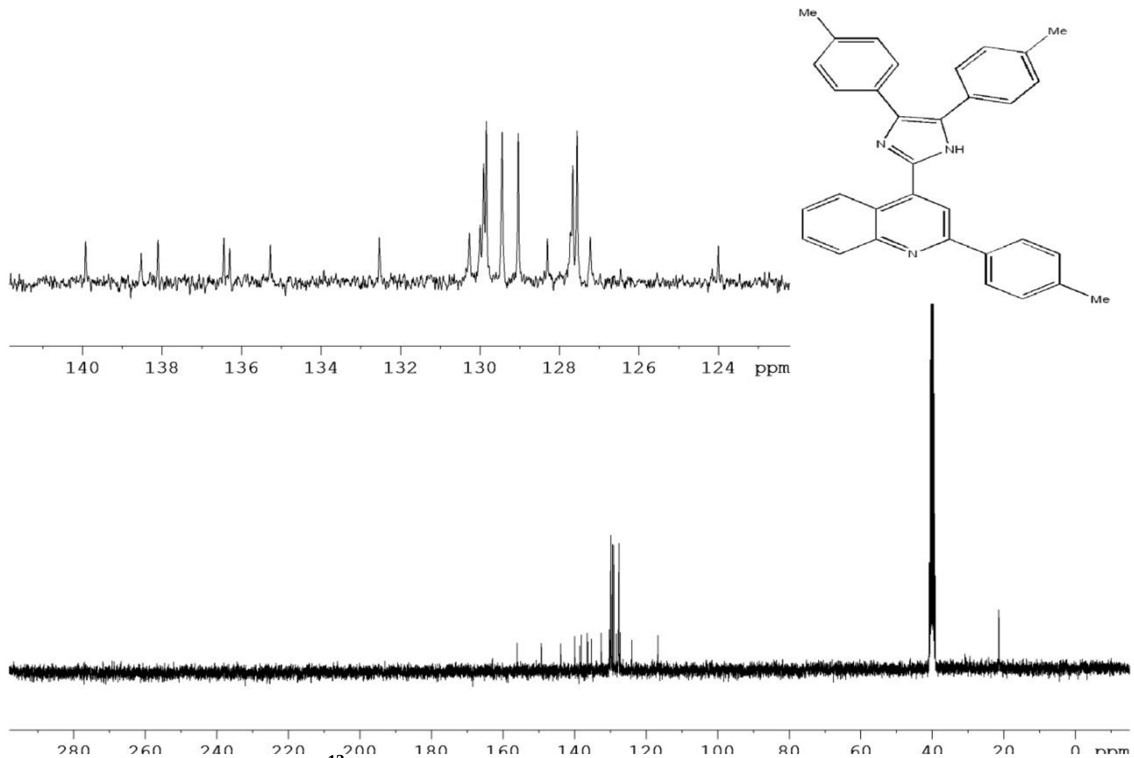


Figure 81. ^{13}C-NMR spectrum of compound [71d] (DMSO-d_6).

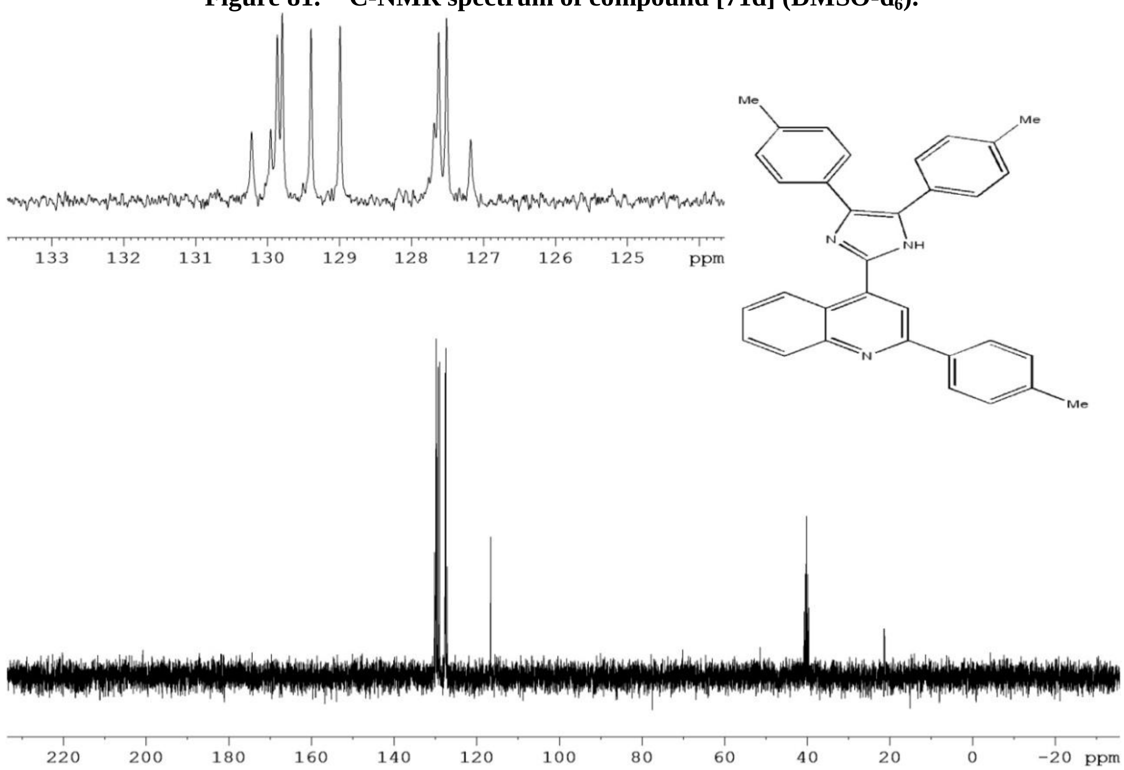


Figure 82. DEPT 135 spectrum of compound [71d] (DMSO-d_6).

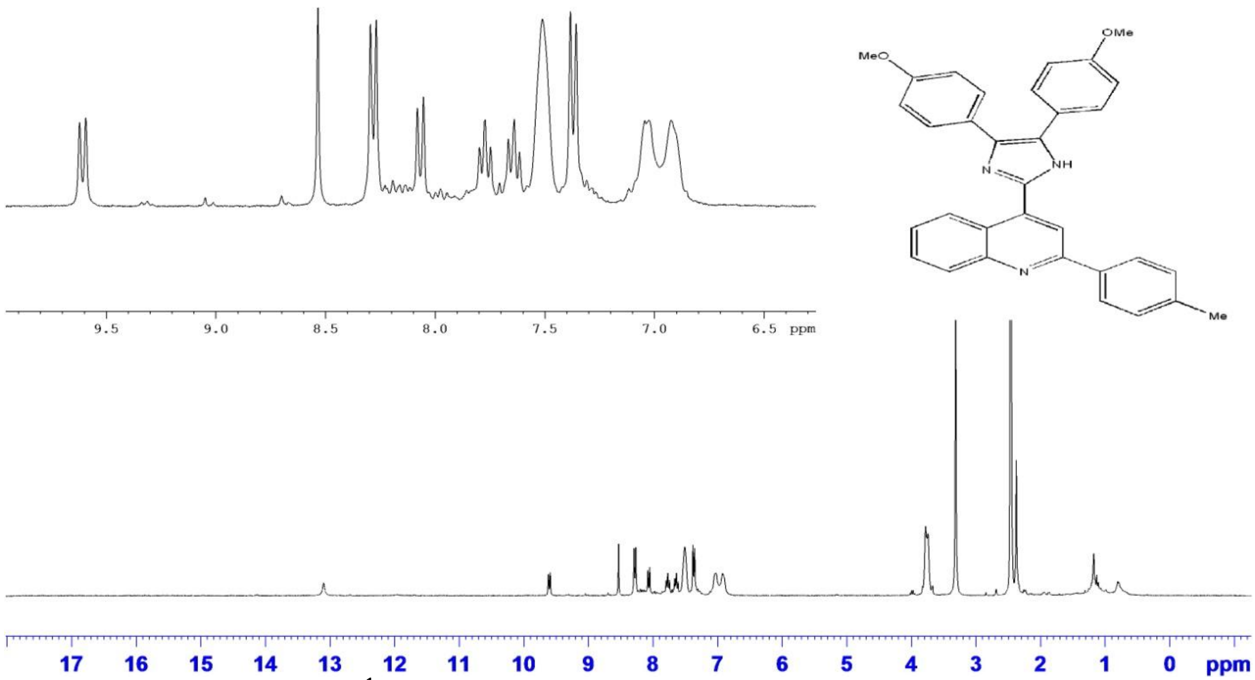


Figure 83. ^{1}H-NMR spectrum of compound [71e] (DMSO-d_6).

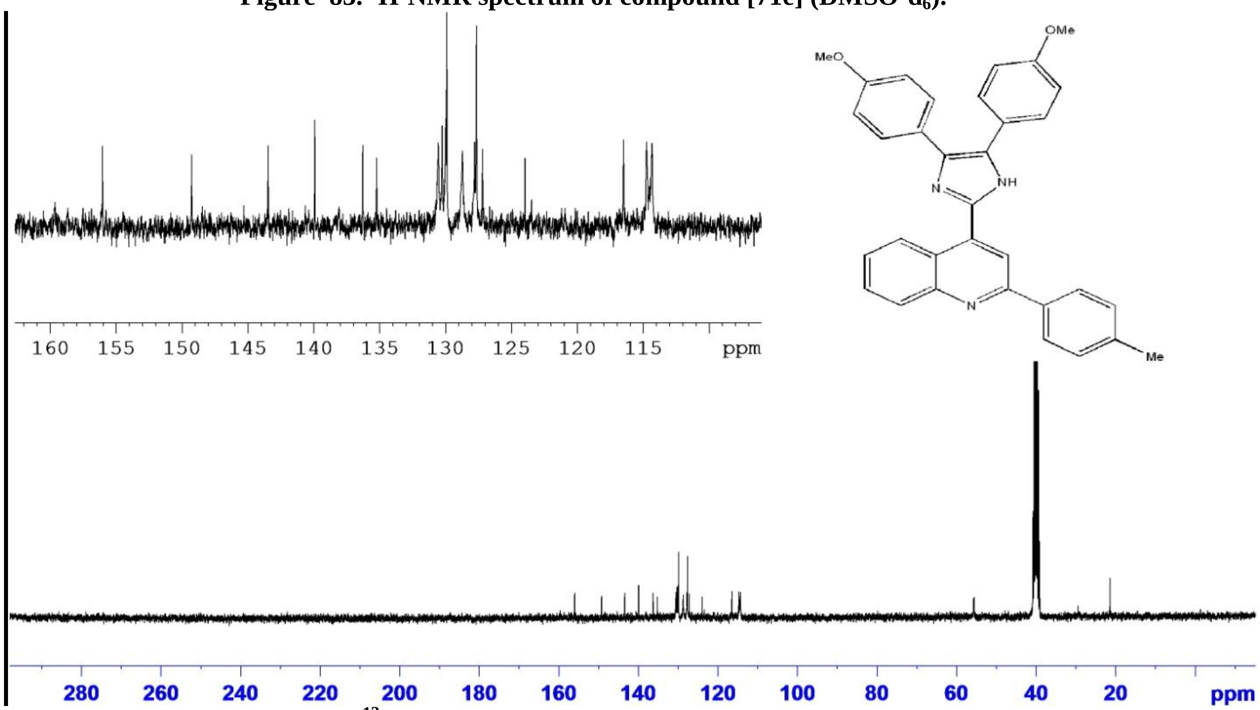


Figure 84. ^{13}C-NMR spectrum of compound [71e] (DMSO-d_6).

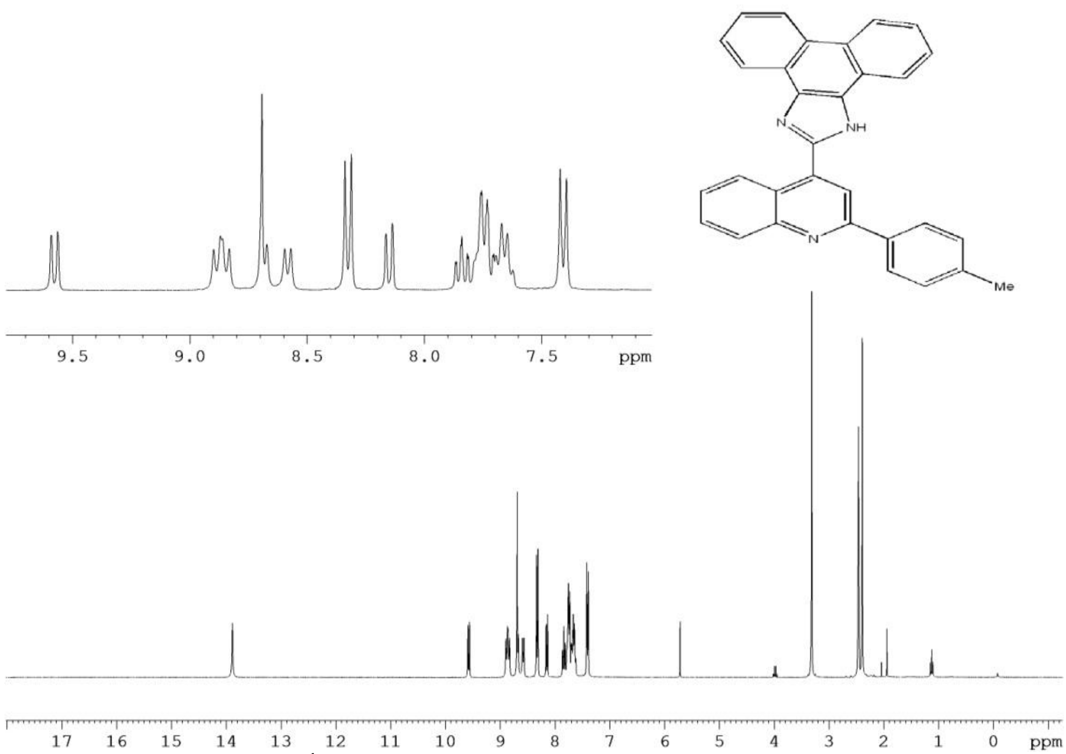


Figure 85. [1]H-NMR spectrum of compound [71i] (DMSO-d$_6$).

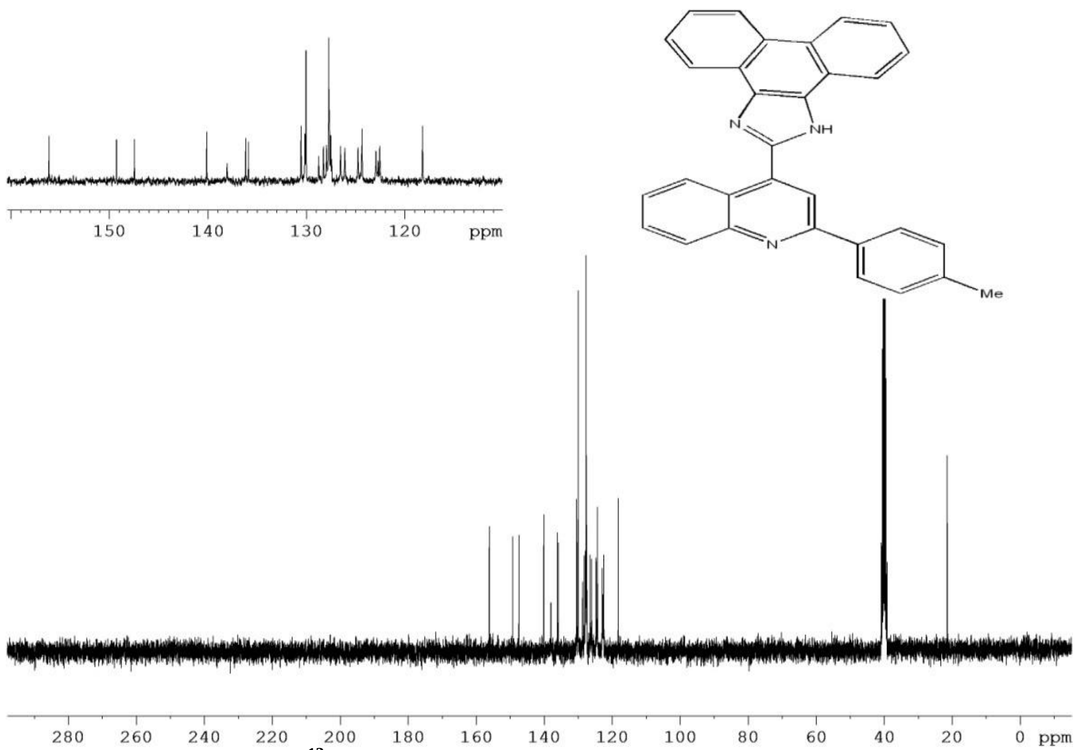


Figure 86. [13] C-NMR spectrum of compound [71i] (DMSO-d$_6$).

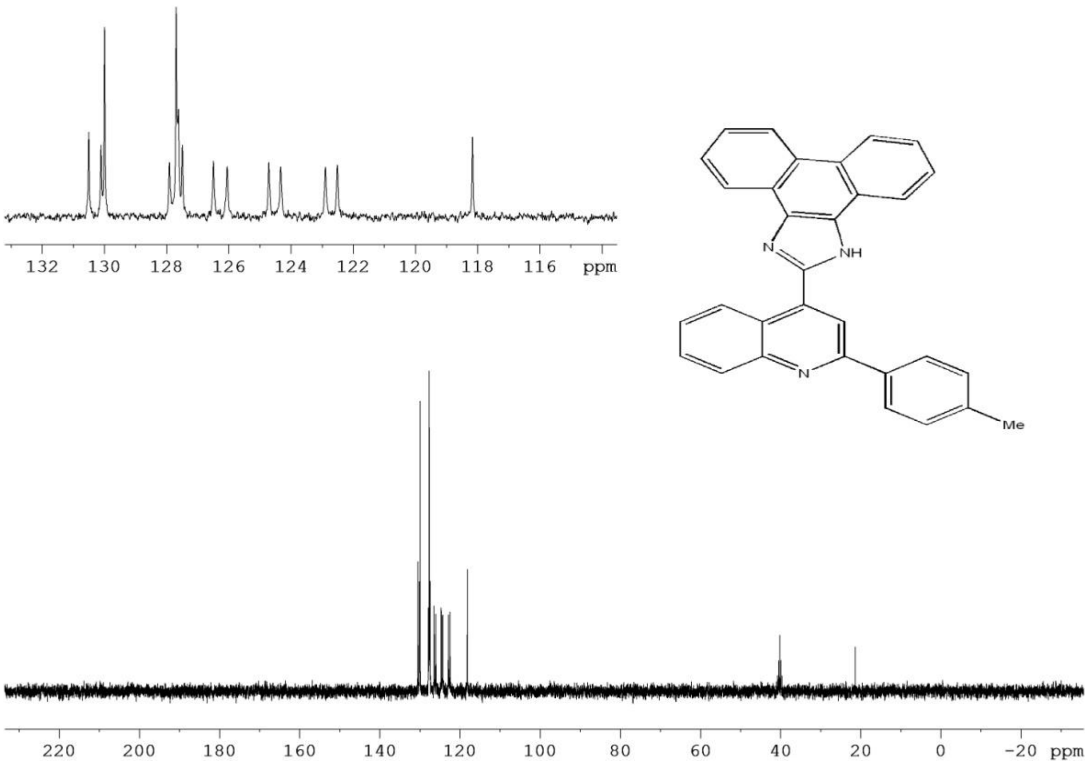


Figure 87. DEPT 135 spectrum of compound [71i] (DMSO-d_6).

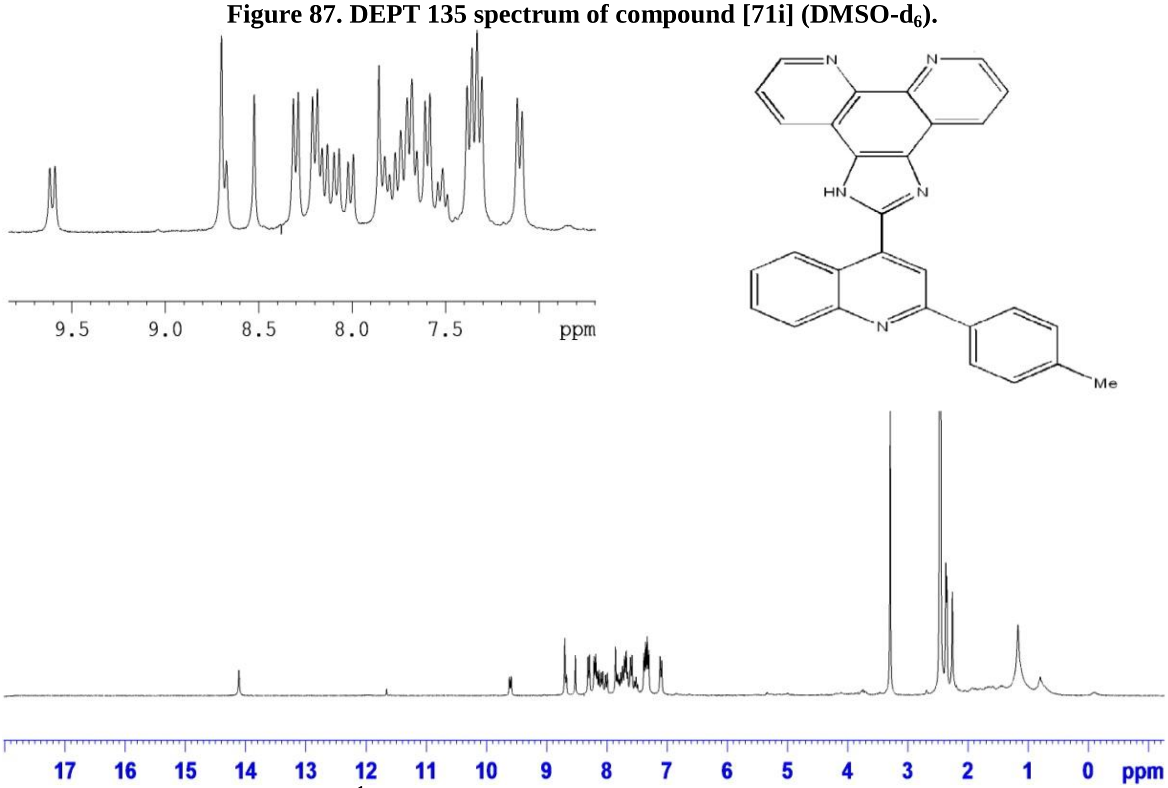


Figure 88. ^{1}H-NMR spectrum of compound [71j] (DMSO-d_6).

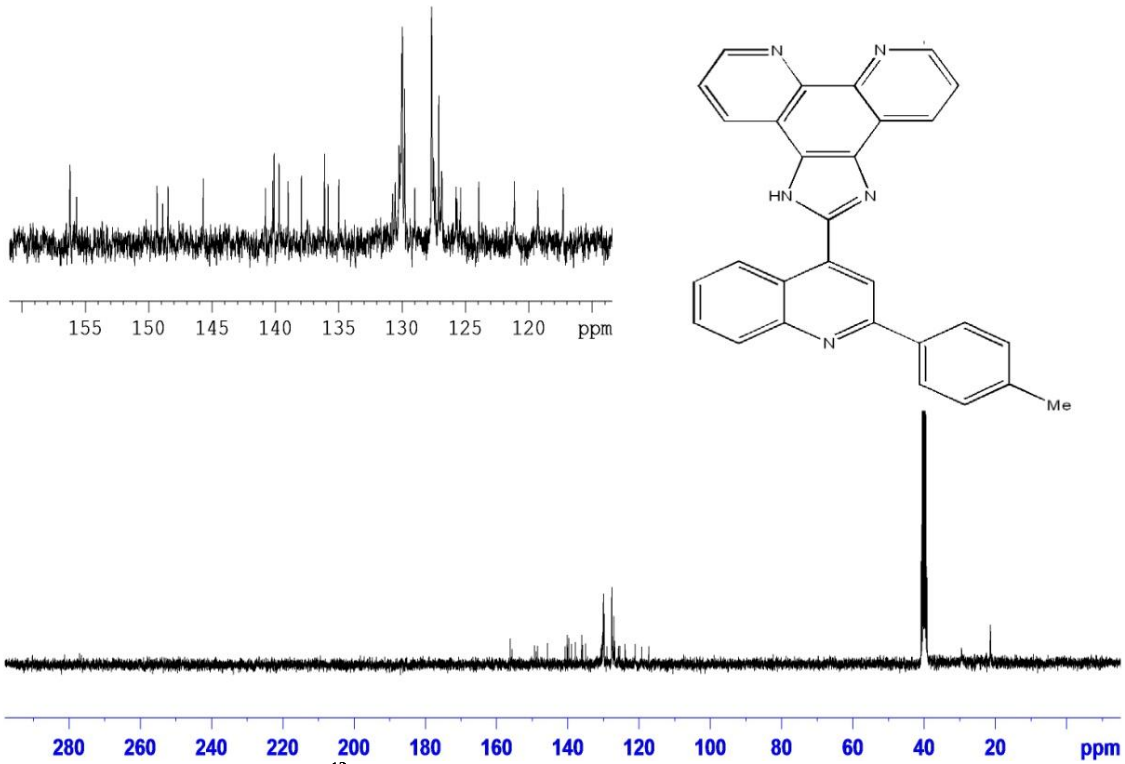


Figure 89. **^{13}C-NMR spectrum of compound [71j] (DMSO-d$_6$).**

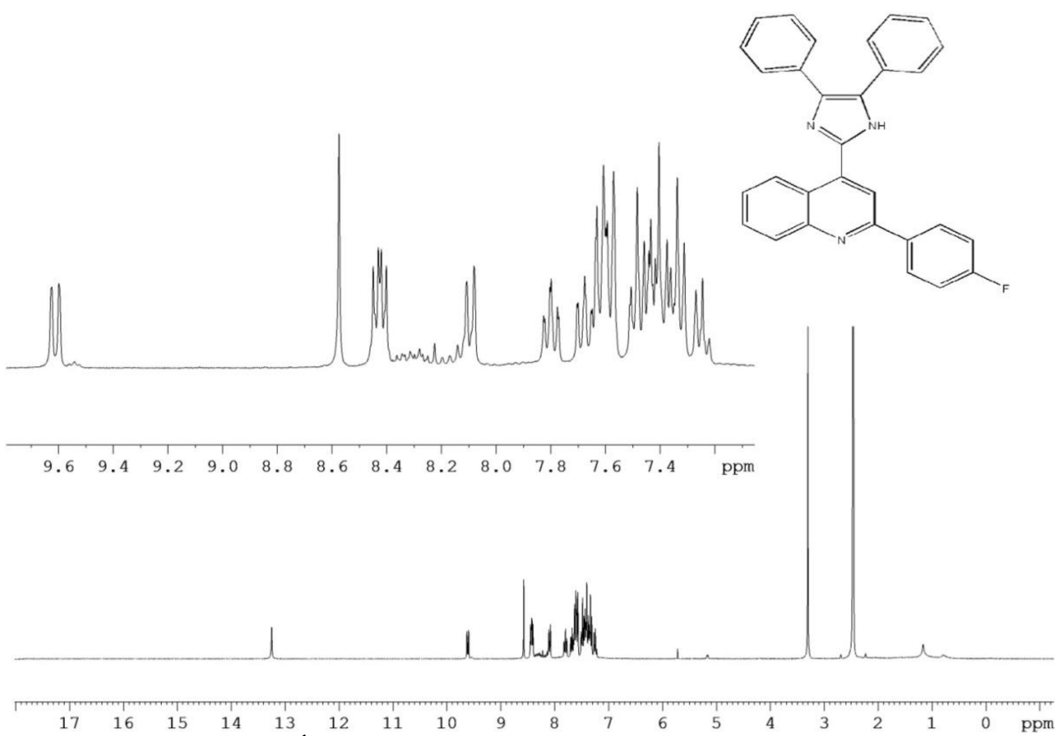


Figure 90. **^{1}H-NMR spectrum of compound [72a] (DMSO-d$_6$).**

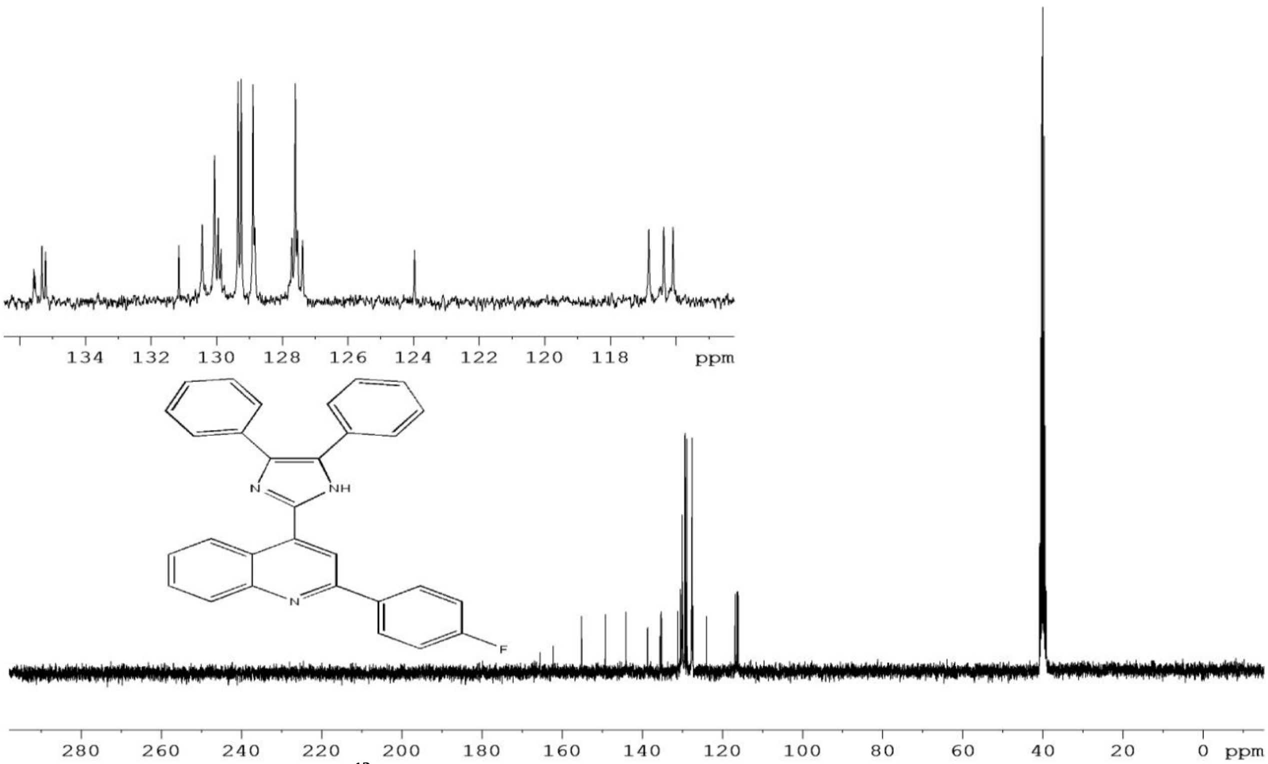


Figure 91. ^{13}C-NMR spectrum of compound [72a] (DMSO-d_6).

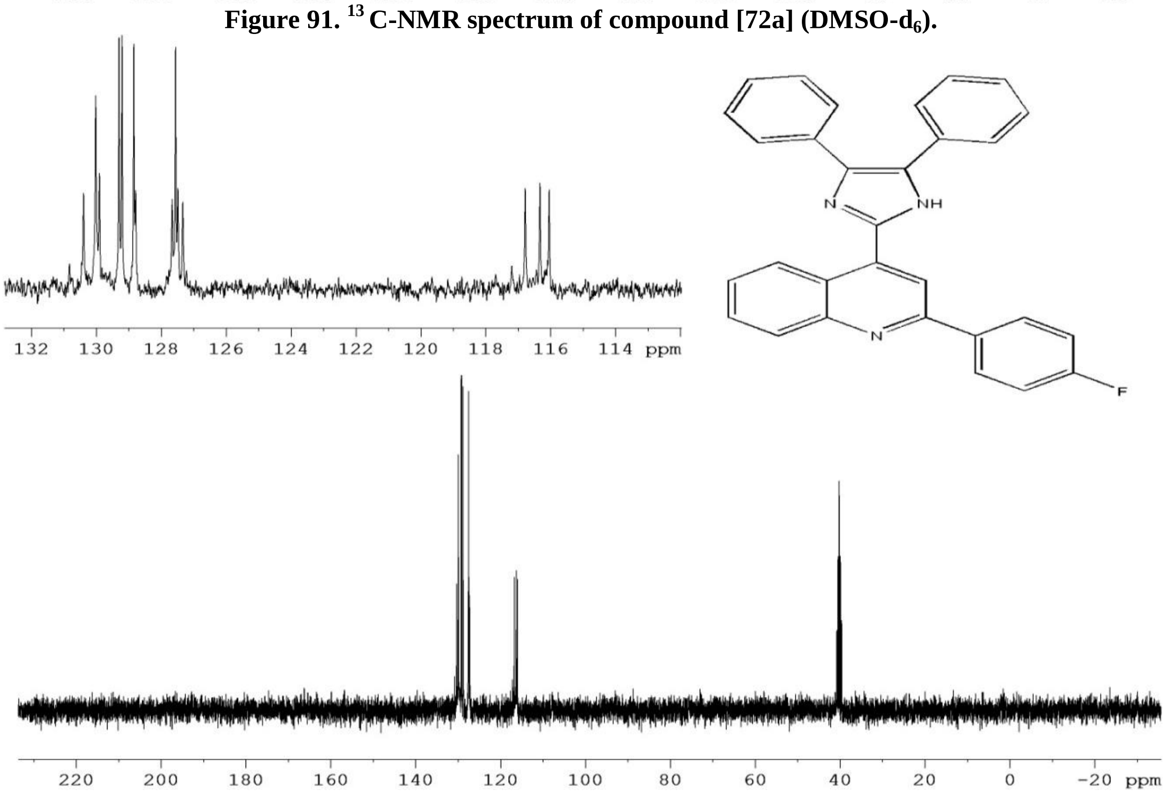


Figure 92. DEPT 135 spectrum of compound [72a] (DMSO-d_6).

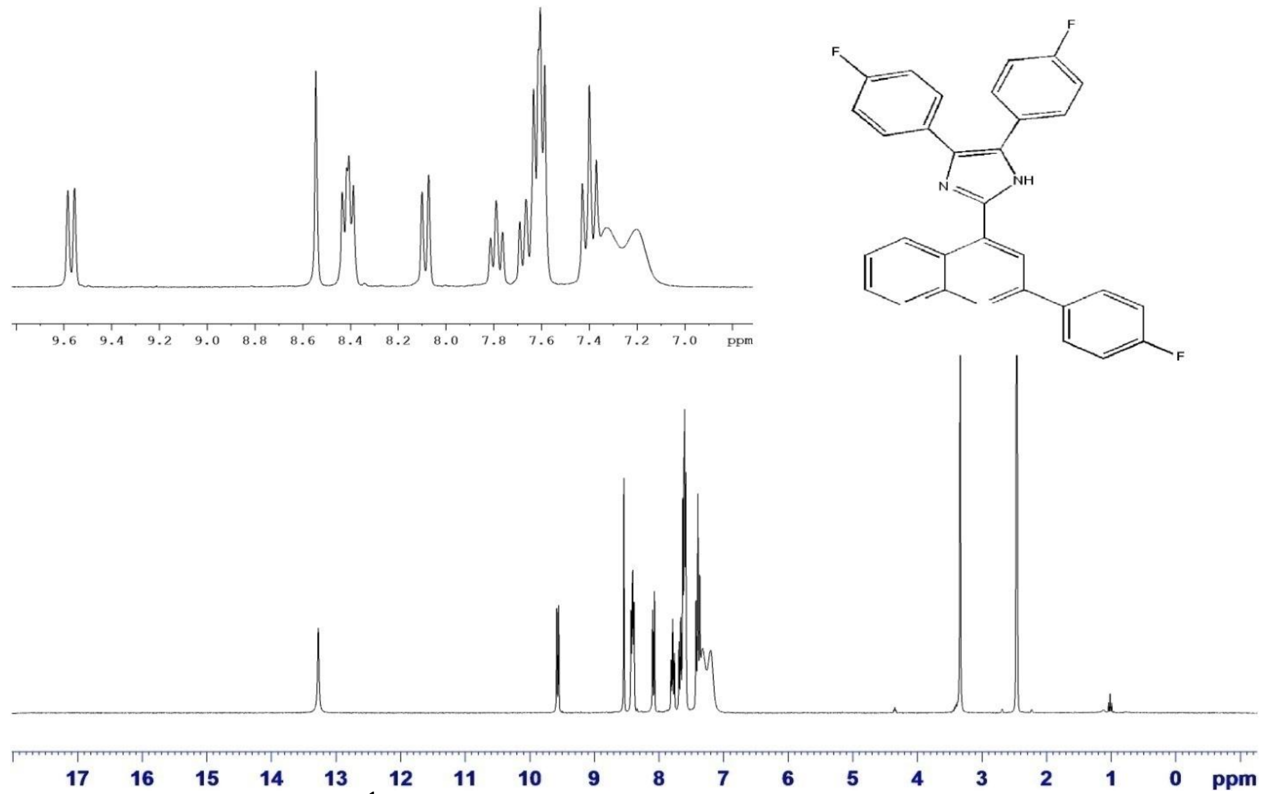


Figure 93. ^{1}H-NMR spectrum of compound [72c] (DMSO-d_6).

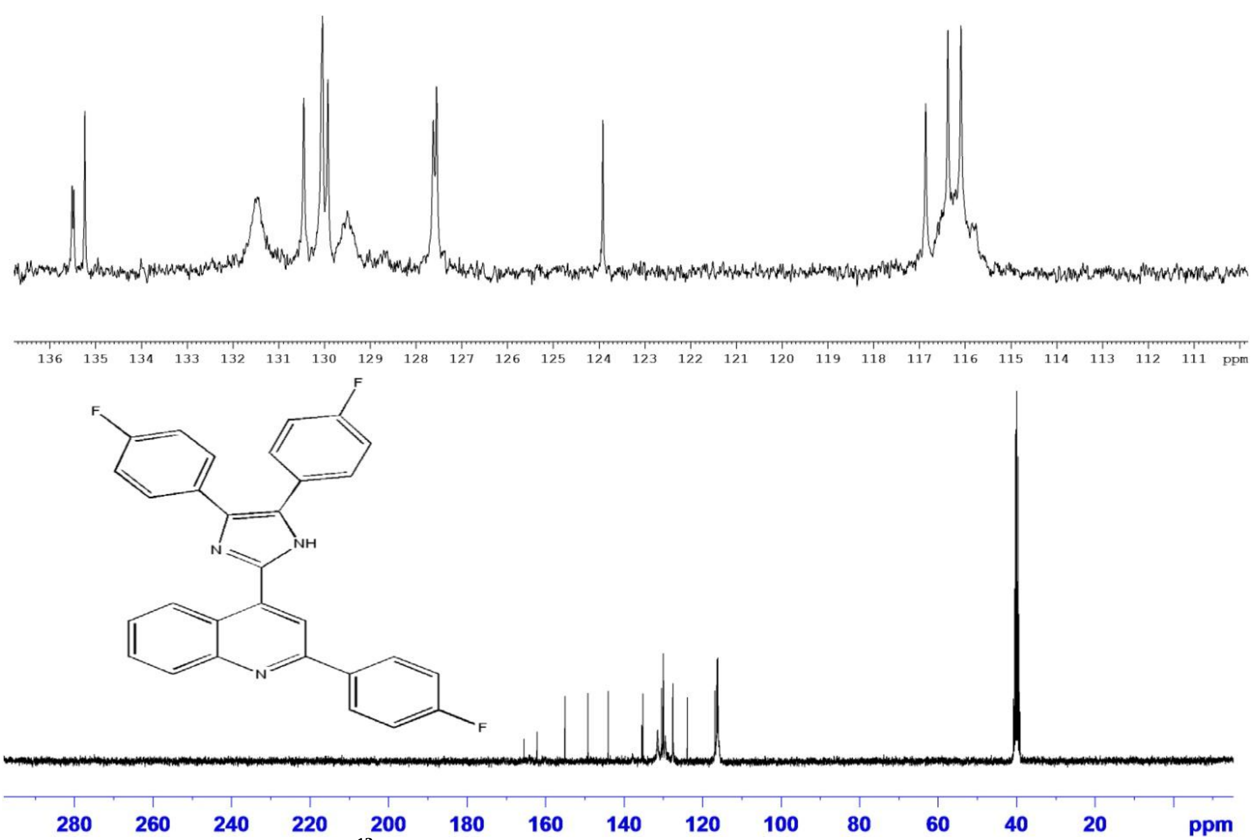


Figure 94. ^{13}C-NMR spectrum of compound [72c] (DMSO-d_6).

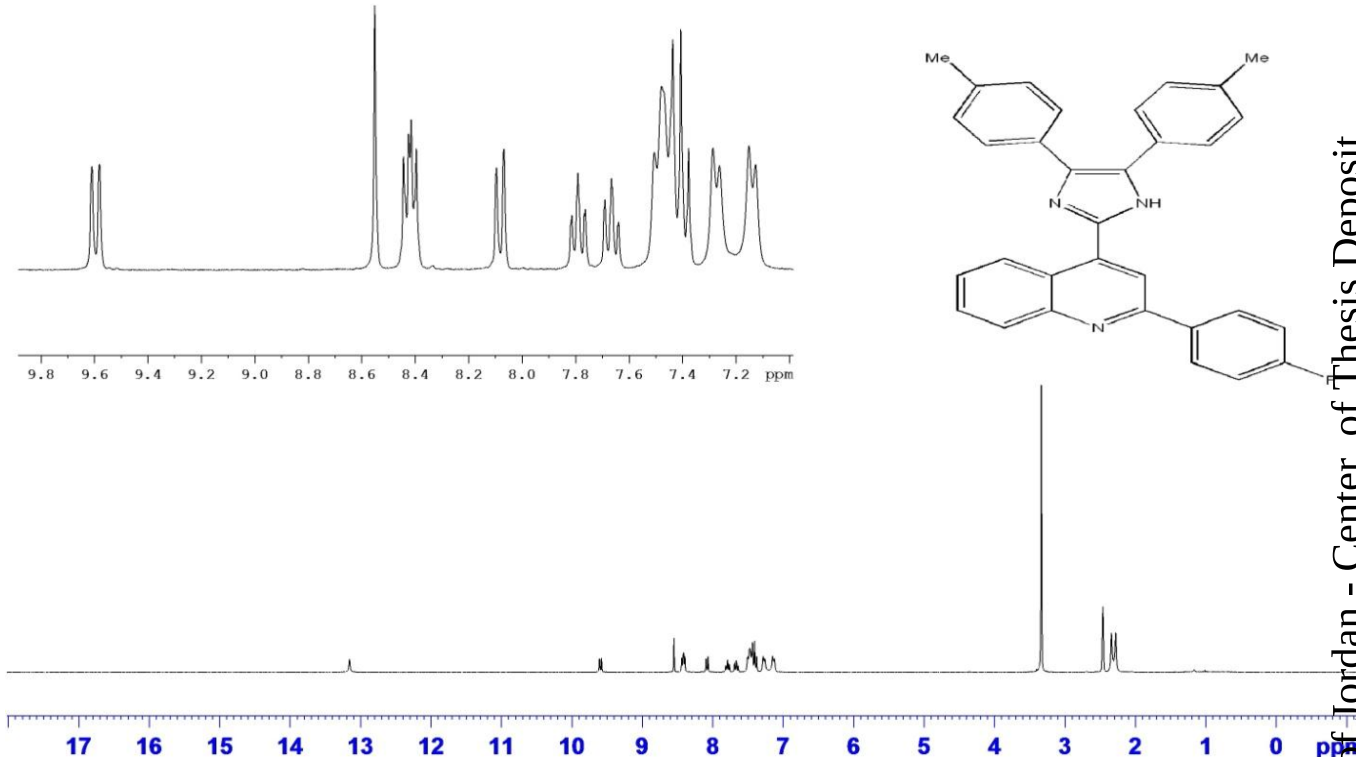


Figure 95. ^{1}**H-NMR spectrum of compound [72d] (DMSO-d$_6$).**

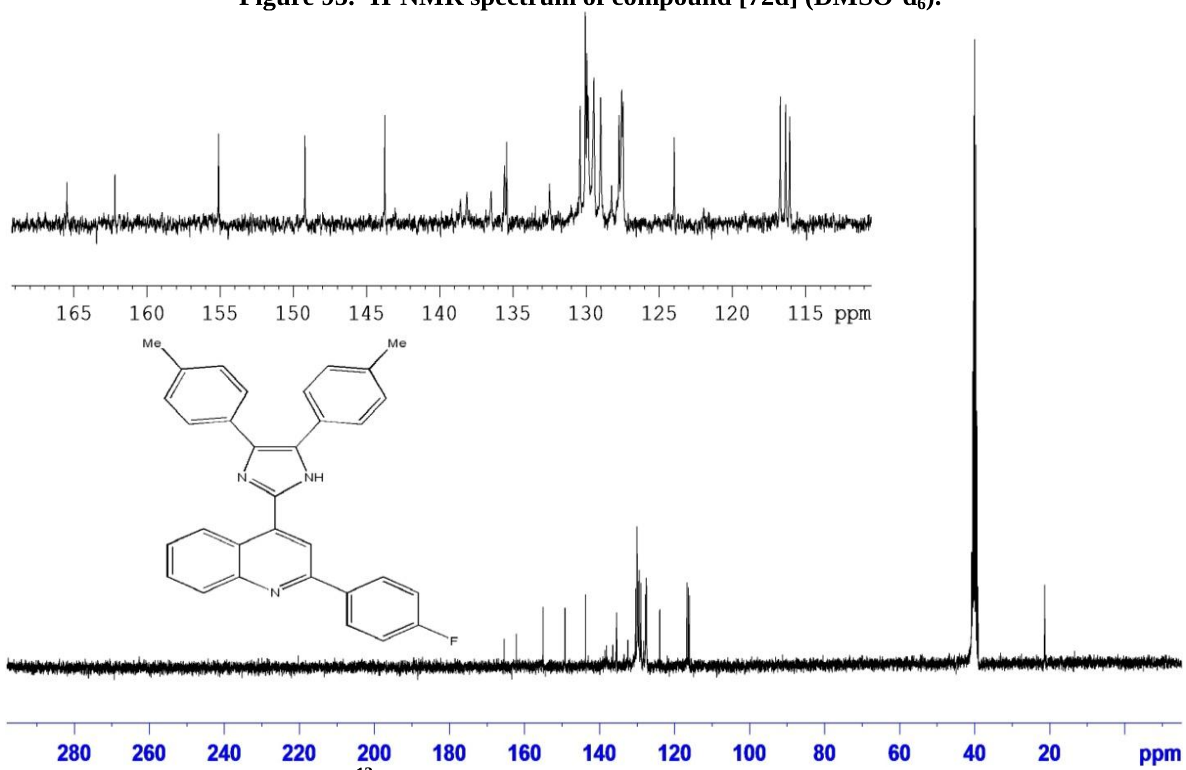


Figure 96. ^{13}**C-NMR spectrum of compound [72d] (DMSO-d$_6$).**

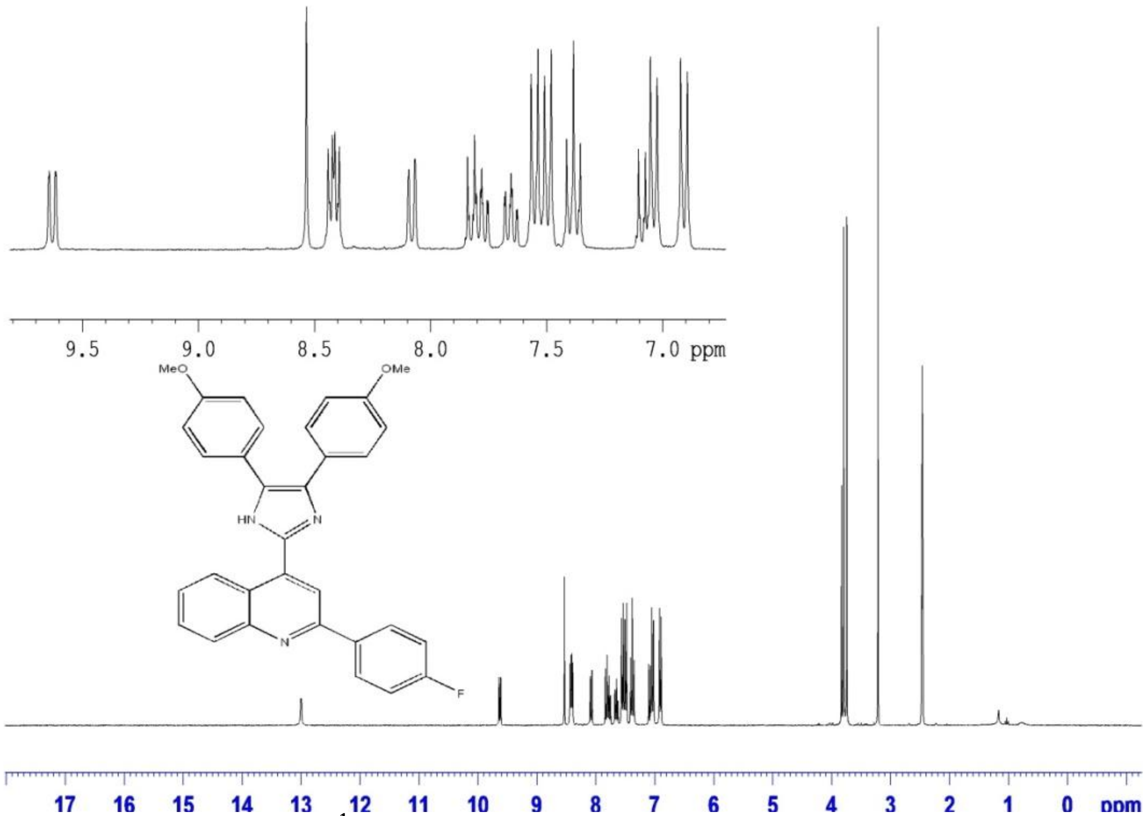


Figure 97. ^{1}H-NMR spectrum of compound [72e] (DMSO-d_6).

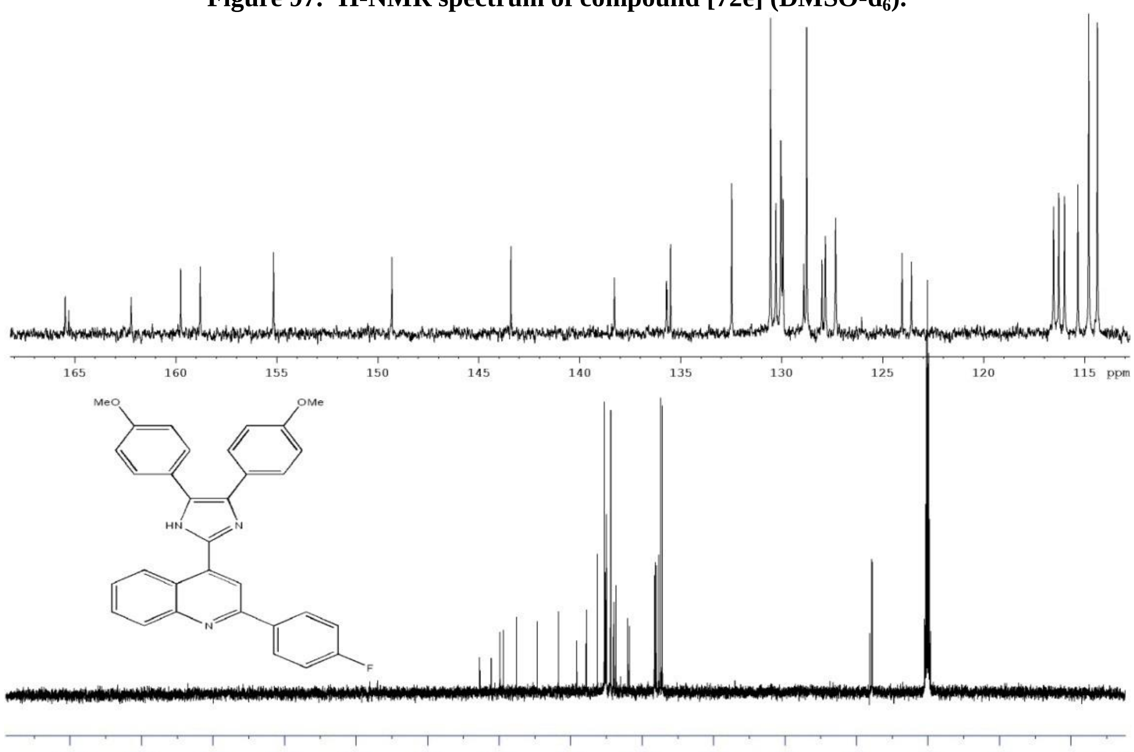


Figure 98. ^{13}C-NMR spectrum of compound [72e] (DMSO-d_6).

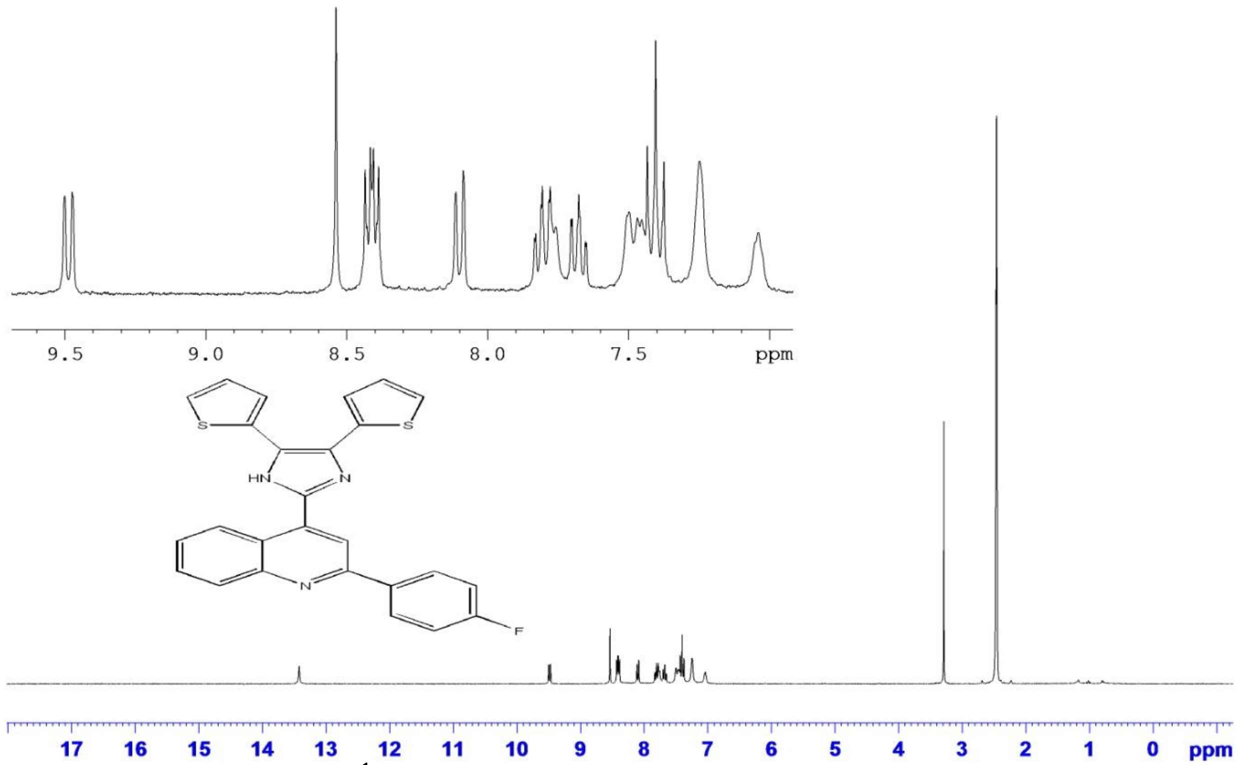


Figure 99. [1]H-NMR spectrum of compound [72h] (DMSO-d_6).

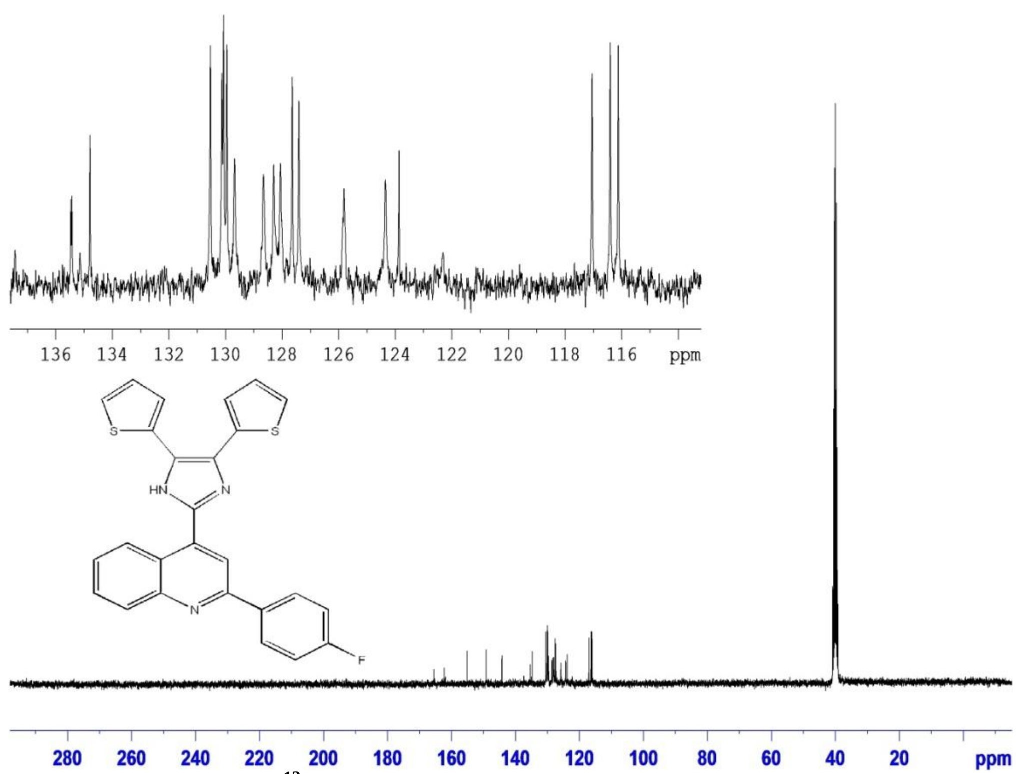


Figure 100. [13]C-NMR spectrum of compound [72h] (DMSO-d_6).

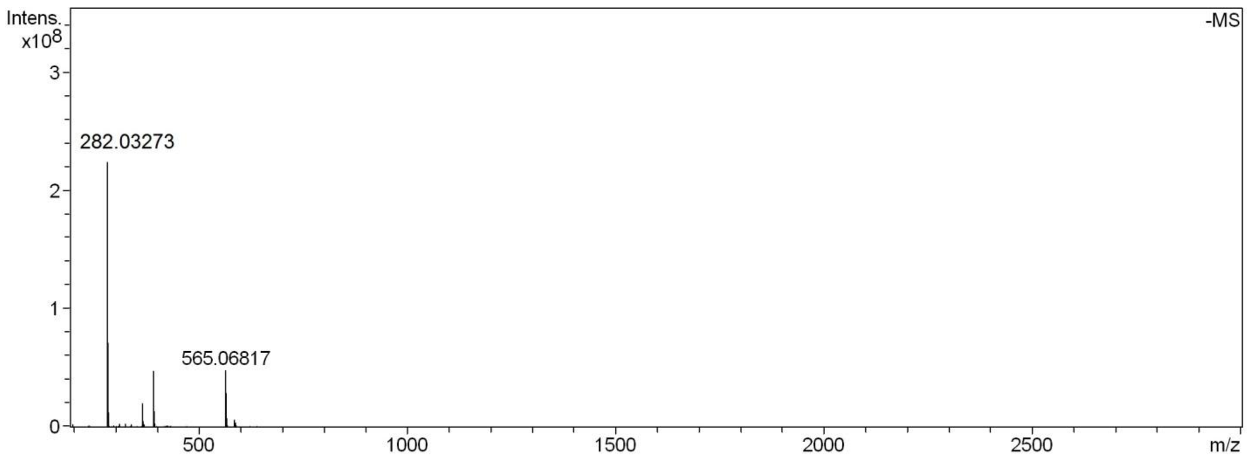


Figure 101. Mass spectrum of compound **64b**

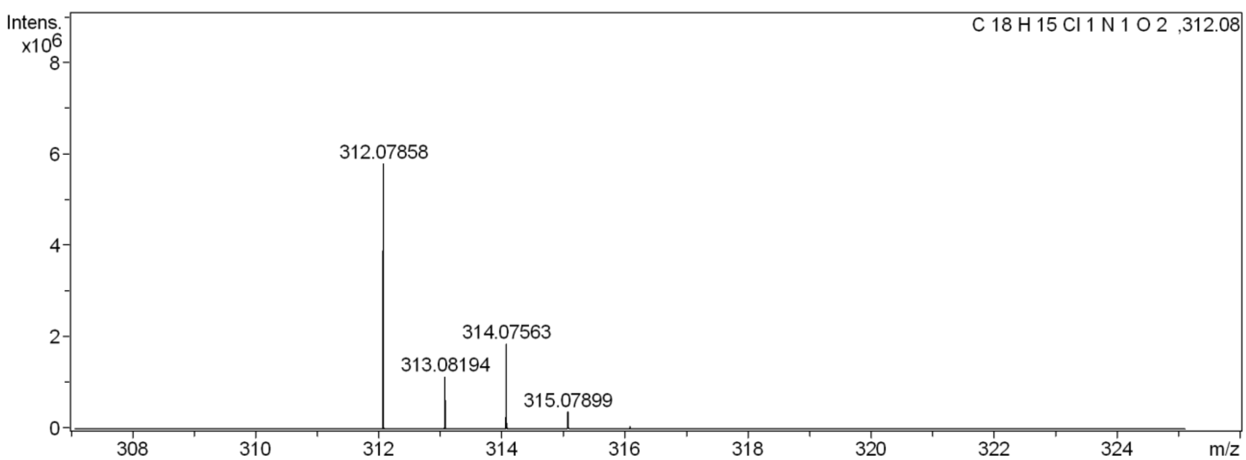


Figure 102. Mass spectrum of compound **65b**

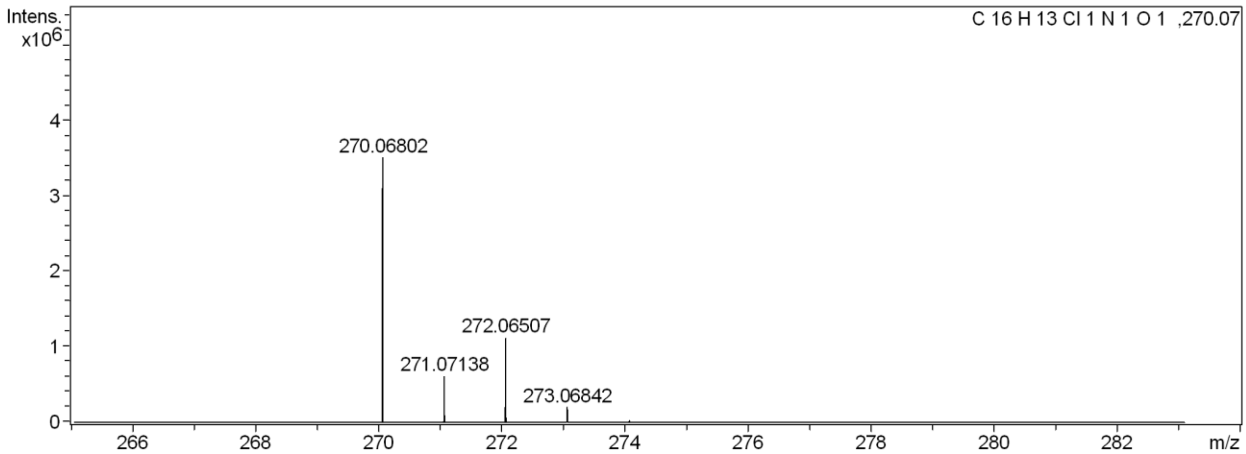


Figure 103. Mass spectrum of compound **66b**

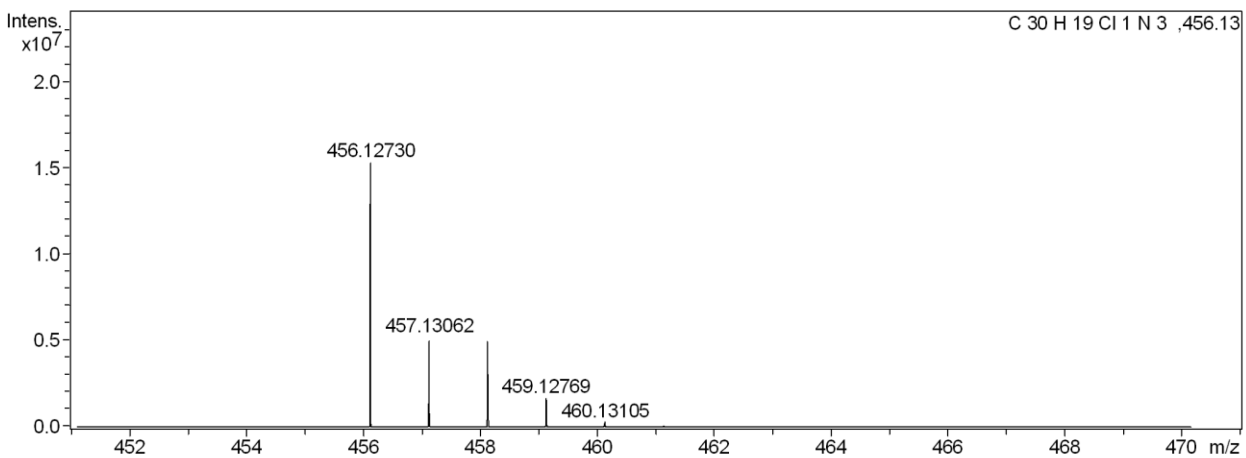


Figure 104. Mass spectrum of compound **70a**

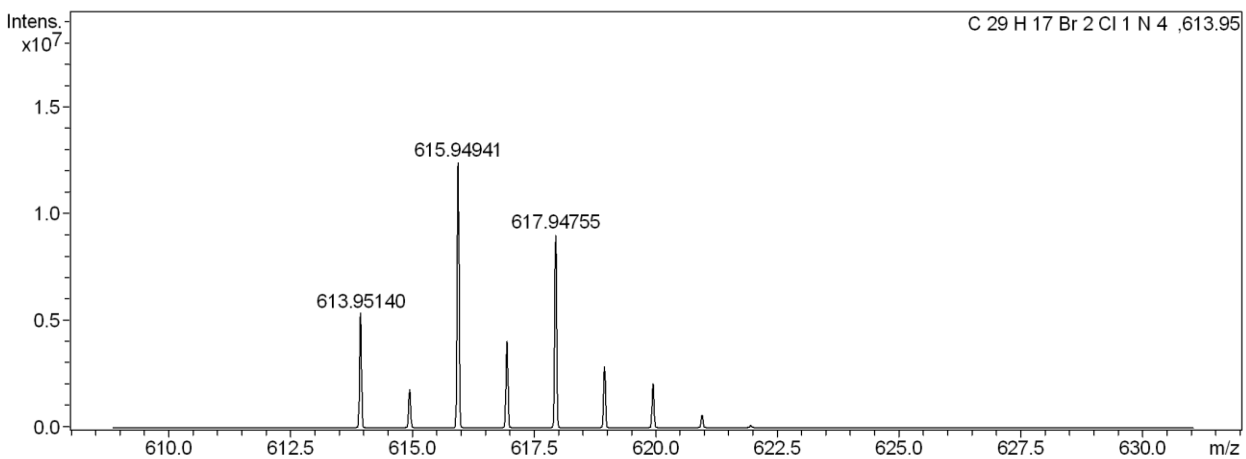


Figure 105. Mass spectrum of compound **70b**

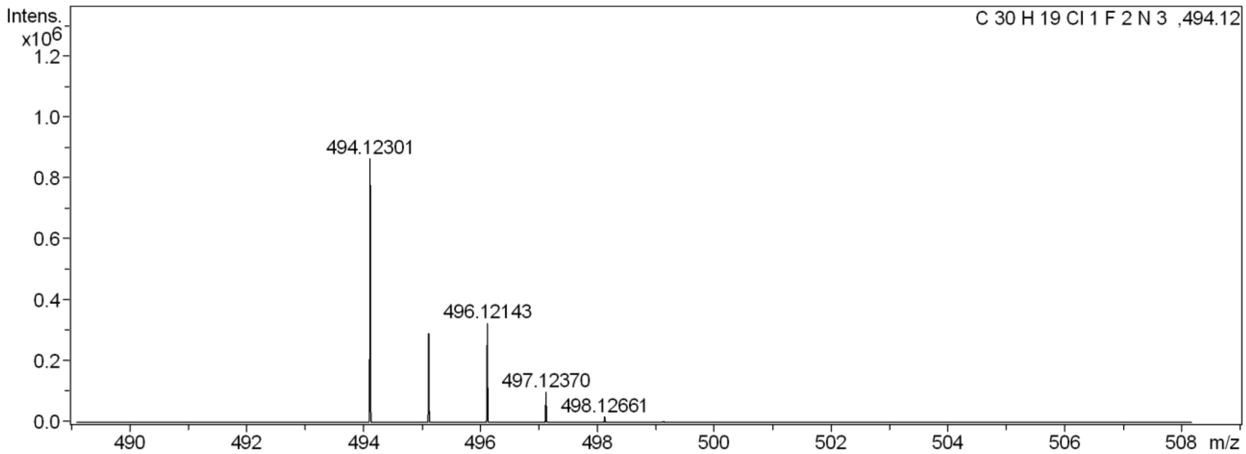


Figure 106. Mass spectrum of compound **69c**

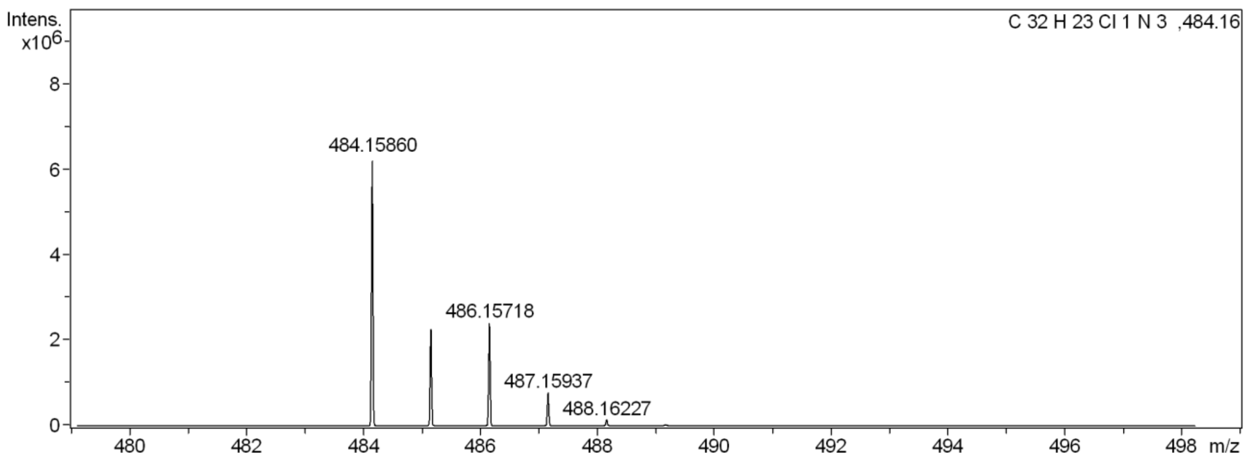


Figure 107. Mass spectrum of compound **70d**

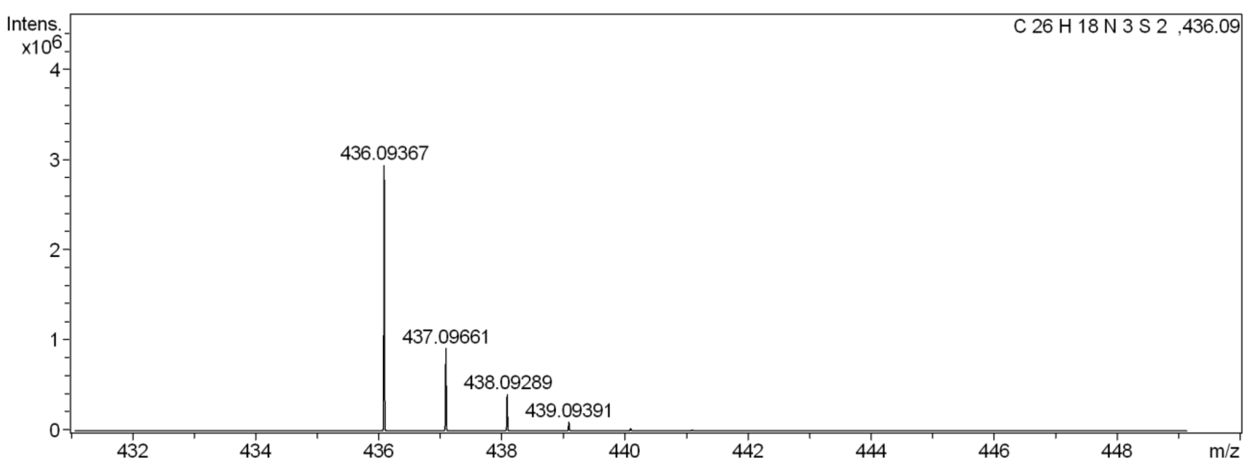


Figure 108. Mass spectrum of compound **69h**

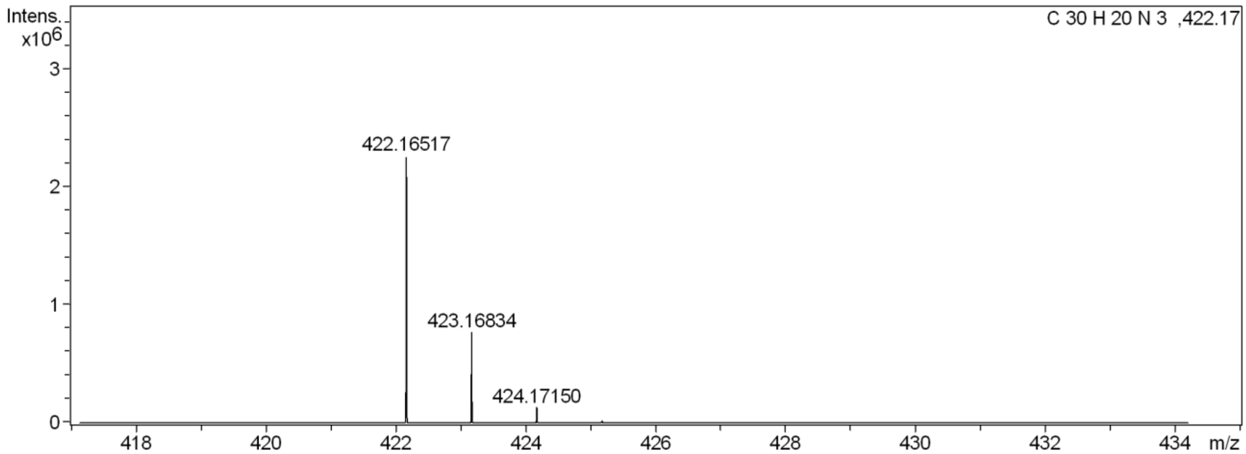


Figure 109. Mass spectrum of compound **69i**

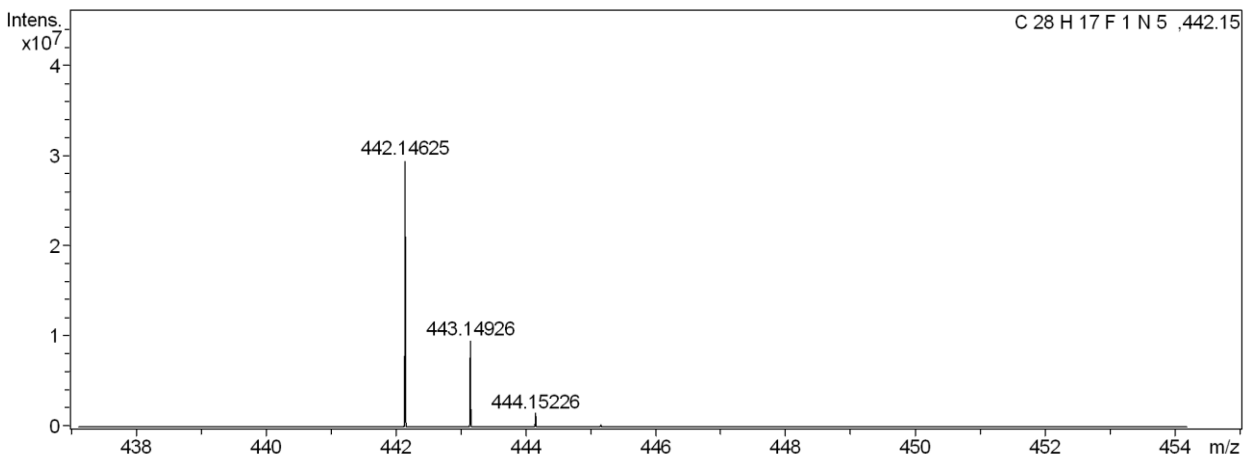


Figure 110. Mass spectrum of compound **72j**

7. Abstract in arabic

استخدام الميكروويف لتحضير مركبات جديده من الاميدازول كوينولين

إعداد
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المشرف
الدكتور رائد عبد الله القواسمه

المشرف المشارك
الأستاذ الدكتور موسى حسن أبو زرقه

الملخص

لقد أبرز التخليق العضوي بمساعدة المايكرويف طريقة فعالة وبسيطة لزيادة الناتج وتقليل زمن التفاعلات الكيميائية. وفي هذه الدراسة تم تصميم مركبات جديدة بناءا على كروموفورات نشطة بيولوجيا. وقد تم تحضير مركبات الاميدازولو كوينولين الجديده باستخدام مفاعل المايكرويف, وتم تشخيص هذه المركبات باستخدام طرق التحليل الطيفية مثل الرنين المغناطيسي ومطياف الكتلة.